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BULLETIN
OF
THE JOHNS HOPKINS HOSPITAL

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TO GRADUATES OF THE JOHNS HOPKINS MEDICAL SCHOOL

The Johns Hopkins Hospital celebrated its Fiftieth Anniversary on May 4th, 5th and 6th. The Committee would have been happy to welcome, on this occasion, all of the graduates of the Medical School, but it was feared that it would be impossible to provide for the large number that might attend if invitations were issued to the entire graduate body. Inasmuch as the Medical School will have its Fiftieth Anniversary in 1943, the Committee decided to make the Celebration entirely a Hospital affair. Accordingly the invitations were limited to present and former members of the Hospital Staff, including Trustees, doctors, nurses, social workers, dietitians, etc. For the public meeting, of course, a large number of Baltimoreans were included in the invitation list.

It is hoped that this explanation will allay any feeling of having been overlooked on the part of the graduates of the Medical School who have not been members of the Hospital Staff.

WINFORD H. SMITH, *Chairman,*
Fiftieth Anniversary Committee.

THE OPENING OF THE HOSPITAL

1889

In the years between 1867 and 1889 The Johns Hopkins Hospital slowly evolved out of a series of ideas communicated by the Founder to his Board of Trustees. Three men in particular are given credit for the effective elaboration of these ideas: Francis T. King, friend of Johns Hopkins and first president of the Board of Trustees; John S. Billings, designer of the hospital buildings and medical adviser to the Board of Trustees; and Daniel C. Gilman, first president of The Johns Hopkins University and first director of the Hospital. When the Hospital was formally opened on May 7, 1889 these three men were the principal speakers and their Addresses are now of unusual historic interest.

A small volume entitled *Johns Hopkins Hospital: Addresses at the Opening of the Hospital* was privately printed in Baltimore in 1889. So far as is known this volume received only a very limited distribution. The Editors of the *Bulletin* have considered it appropriate, therefore, to republish the opening Addresses in the following pages. A brief account of the opening exercises, together with Johns Hopkins' letter of instructions to his Board of Trustees, may be found in Volume I of this *Bulletin* (1889). The Addresses delivered at the Twenty-fifth Anniversary Celebration appeared in Volume XXV (1914).

OPENING ADDRESS[1]

FRANCIS T. KING

President of Board of Trustees

It is my pleasant duty, in behalf of the Trustees of the Johns Hopkins Hospital, to offer you a cordial welcome, and to express our high appreciation of the interest in our work which is manifested by your presence here to-day.

It cannot be a matter of small or temporary importance that brings to this opening the chief executives of our State, and our City, so many of our distinguished men in all branches of the public service, so many well-known professional men from distant cities and countries, and so many of our own most prominent and public spirited citizens; and it gives us a renewed sense of our responsibilities and duties to find that we are to give an account of what we have done in the past and what we hope to do in the future to such an audience as we see before and around us.

It encourages us to hope and believe that the trust which has been confided to us is one not only of local but of national and even of international importance, and we have abundant evidence in the many letters which have come to us from beyond the sea, that the opening of this hospital and the commencement of its philanthropic, educational and scientific work, is a matter which interests many men and women in Europe as well as in all parts of this country.

Johns Hopkins did not leave a hospital; what he did leave was a complicated piece of machinery in the form of various investments capable of evolving the power required to construct and maintain a hospital, for in this sense money is power. This machinery requires constant adjustment and looking after, and for this part of the work the Trustees are solely responsible.

When I tell you that these seventeen buildings have been constructed and furnished, and these fourteen and a half acres enclosed

[1] From *Johns Hopkins Hospital: Addresses at the Opening of the Hospital.* Privately printed. Baltimore, 1889.

and beautified as you see them to-day, not only without taking a dollar from the principal placed in the hands of the Trustees, but with an actual increase of the endowment by judicious investments by the sum of $113,000, I think it may be justly claimed that the Trustees have not failed in this part of their duty.

The speakers who are to follow me will tell you of the plans of the hospital, of the objects which have been kept in view in the preparation of the methods adopted to secure the best possible conditions for the treatment of the sick and wounded who come to it, of its relations to medical education, to improvement of the science and art of medicine, and to the other great trust of Johns Hopkins with which it is so intimately connected, namely the university.

I will therefore devote my closing remarks to one or two personal reminiscences of the man to whom we owe the magnificent possibilities of his two great gifts.

I need not speak of the birth, education and business career of Johns Hopkins, with which most of you are familiar, as he was a native of this State.

What were the motives which led him to found his two great trusts, each with an endowment of nearly three millions and a half of dollars? Was it the act of a man of great wealth without children, who near the close of life wished to build a monument to his memory? No, not at all; it was done conscientiously, with all the deliberation, judgment and grasp of subjects which characterized him through life, first as a successful merchant, then as a banker.

I remember, many years ago, while spending an evening at Clifton, I heard Johns Hopkins say, in reply to a question put to him by an intimate friend of his own age, why he had never made a will, that he looked upon his wealth as a gift, for which he was accountable; that it grew and piled up from a small beginning, he hardly knew how; but he was sure it was given to him for a purpose, and he did not believe he would die before he was given to see how he should dispose of his estate. "This wealth," he repeated, "is my stewardship."

Again, when his Trustees arranged to visit the hospitals of Philadelphia, New York, and Boston he was asked to accompany them; his reply was, "You surely do not want to parade me around the country. I would not for a moment think of going; it would be in very bad taste,

to say the least of it. I have carefully chosen my Trustees and have committed every thing to them. I will furnish the means and they must build the Hospital."

Johns Hopkins purchased this site himself, which then consisted of the grounds of the Maryland Insane Asylum, two large lots and seventeen dwellings, in all fourteen and a half acres of ground in an improved portion of the city, closing two public streets, thus at once determining the magnitude and character of his Hospital.

Let Johns Hopkins again speak for himself in the words of his letter to his trustees, which show the wide scope of his interest in all conditions of mankind:

"You shall receive into the Hospital the indigent sick of this city and its environs without regard to sex, age or color, who may require surgical or medical treatment, and the poor of this City and State, of all races, who are stricken down by any casualty.

"You will also provide for patients who are able to make compensation for the room and attention they may require, and thus be enabled to afford to strangers and to those of our own people who have no friends or relatives to care for them in sickness, and who are not objects of charity, the advantages of careful and skilful treatment.

"It will be your duty hereafter to provide for the erection upon other ground of suitable buildings for the reception, maintenance and education of orphan colored children, for which purpose I desire that you shall apply the yearly sum of twenty thousand dollars, or so much thereof as may be necessary."

I wish to say on behalf of the Trustees a few words of recognition to all who have labored to bring these plans to their conclusion; to the medical adviser whose invaluable services have covered more than ten years; to the President of the University, who has so ably aided in organizing; to the architects and builders, and to those who have had but occasional opportunities to serve us, but who have freely contributed their wisdom and experience whenever called upon, and especially to the physicians and surgeons, the managers of other hospitals, the superintendents of training schools for nurses, and to many others, at home and abroad, whose kind co-operation has been most serviceable.

Many of these friends are within the sound of my voice; others far

away; none are forgotten; not a few sent us letters which show their lively interest in this occasion.

As Johns Hopkins was brought up by godly parents—members of the Society of Friends—I should have been glad if we might have heard the voice of Whittier, the Quaker poet, but in the letter which I hold in my hand he pleads his age and illness as an excuse for his silence. He expresses his pleasure in seeing that the wise and benevolent design of the founder has been so well carried out, and his hope that the example of Johns Hopkins will not be lost upon his country.

To the words of his letter I will venture to add this verse which he wrote for another occasion, but which is equally appropriate to this.

> "Not vainly the gift of its founder was made;
> Not prayerless the stones of its corner were laid;
> To Him be the glory forever!—we bear
> To the Lord of the harvest our wheat with the tare;
> What we lack in our work, may He find in our will,
> And winnow in mercy our good from the ill!"

THE PLANS AND PURPOSES OF THE JOHNS HOPKINS HOSPITAL[1]

JOHN S. BILLINGS, M.D.
Surgeon, United States Army

The third paragraph of the letter of instructions communicated by Johns Hopkins to the trustees whom he had chosen to carry out his plans for a hospital in the city of Baltimore, states that "it is my wish that the plan . . . shall provide for a hospital which shall, in structure and arrangement, compare favorably with any other institution of like character in this country or in Europe." What do you suppose the writer was thinking of when he penned that sentence? Had he in view any definite ideal, any mental picture of the institution which he proposed to establish, or was it merely an expression of a desire to give to his city the best thing that could be devised? I have read that letter many times, have heard much of the ideas, hopes, and wishes which were expressed in the numerous conversations which preceded its preparation, and it seems to me that the writer had an ideal, and not a mere vague desire—an ideal which was no doubt somewhat misty, but which did not correspond to any existing hospital, and one which he did not attempt to define except in a few prominent points to which I shall presently refer. In most respects Johns Hopkins took the same course with his hospital which he did with his university, and deliberately refused to trammel with specific directions those whom he had chosen to carry out his plans; but this letter of instructions indicates, nevertheless, a conception of much more definite character, and one which had been the subject of more discussion and reflection than his scheme for a university. Whether this be so or not, I am at all events sure that his trustees have endeavored to comply with this letter of instructions, and to do so in the broadest and best sense of the words.

The beginning of the results we have before us to-day—results

[1] From *Johns Hopkins Hospital: Addresses at the Opening of the Hospital.* Privately printed. Baltimore, 1889.

which even now are not confined to these particular aggregations of bricks and mortar, as will be presently explained, and the end of which will be, as we hope and believe, to make life happier for millions now living and yet unborn. Only those who took part in the early deliberations of those charged with this trust can fully realize the anxieties, the doubts, the manifold perplexities which at first attended their decisions and movements. Only one or two of them had any knowledge of hospital matters; most of them were business men, bankers, lawyers, judges, railway managers, men who knew something of the management of men and money, but who were now brought face to face with a new problem—viz., how to build, organize, and manage a hospital so that it should compare favorably with any other hospital in this country or in Europe.

To "compare favorably with," what does that mean? It is a peculiar phrase, which, coming from a shrewd business man and a member of the Society of Friends, signifies, I think, to excel, if possible; at all events, that is the safest interpretation. And it was not this or that hospital which was to be surpassed or equaled, but all other hospitals in this country or in Europe; Africa, Asia, and Australasia being put out of the question. It was a large contract.

The location was fixed—that had been done by Johns Hopkins; but they had to decide whether the structures to be erected should be temporary or permanent, of wood, brick, or marble, in one large building or in many, and many other like points, before even the preparation of plans could be commenced. They followed the instructions of the donor and got advice, of which a great abundance was available. They visited the large hospitals of our eastern cities, employed five men, supposed to be skilled in hospitals, each to write an essay giving his plans and suggestions, published these essays in a book which had a wide circulation, and studied the criticisms and reviews to which this book gave rise.

Having duly considered the multifarious and widely divergent suggestions thus obtained, they finally selected one of the essay writers and asked him if he was satisfied with his own plans now that he had seen the others and the published criticisms upon them. He promptly said that he was not, whereupon they asked him to try again and do better. He set to work, aided by the architect of the board, and

the result was a set of sketch plans which he took abroad and obtained much counsel and criticism on, examining at the same time the model hospitals of Europe. He was much less satisfied with the sketch plans when he came back than he was when he started, and again the building committee, the architect, and himself reviewed the whole matter, and finally settled on the general arrangement which you will see to-day. Many details remained to be worked out; even the façades had not yet been designed; but the general scheme was settled, and the rest was comparatively easy for the time being.

Let us now for a few moments consider the broad general principles which governed the trustees in the adoption of this plan. The first hospitals were established to give shelter and food to the sick poor, especially those who gathered in cities. Gradually physicians found that they could learn much in these aggregations of suffering and that they afforded the means of teaching others; but this last use of them is only about two hundred years old. Gradually, also, it came to be known that the knowledge thus obtained in the care of the sick poor was of use in treating the diseases of the well-to-do; and finally, within the last twenty-five years or so, people are beginning to find out that when they are afflicted with certain forms of disease or injury they can be better treated in a properly appointed hospital than they can be in their own homes, no matter how costly or luxurious these may be. In the hospital they can have not only all the comforts of home, but more; not only skilled medical attendance and skilled nursing, but the use of many appliances and arrangements specially devised for the comfort and welfare of the sick which can hardly be found in any private house, and also freedom from noise and many petty annoyances, including in some cases too much sympathy and in others too little. This hospital, then, is to provide for the rich as well as for the poor; for those who can, and ought to, pay for the help given, as well as for those who can not.

A second cardinal principle to be observed in such a hospital as this is, that it shall do as little harm as possible. A hospital may do harm by its foul air, by spreading contagious disease among its inmates, by neglect or carelessness of its nurses or attendants; and in years gone by hospitals have, no doubt, caused nearly as much sickness as they have relieved. This is now rarely the case, and in this hospital the arrange-

ments for ventilation, isolation, and nursing are such as to entirely do away with this danger. There is another danger connected with free hospitals and dispensaries which is of quite a different kind and to which I can here only allude, namely, the danger of promoting negligence, shiftlessness, laziness, and vice by offering free relief from their consequences—the danger of pauperizing people. This is a danger connected with organization and management rather than with construction, and I can only say here that it has been foreseen and will be as far as possible guarded against.

The third principle to be kept in view in such a hospital as this is, that it should provide the means of giving medical instruction, for the sake of the sick in the institution as well as of those out of it. It is well known to those familiar with the subject that the sick in a hospital where medical instruction is given receive more constant, careful and thoughtful attention than do those in a hospital where no such instruction is given. The clinical teacher must do his best; keen eyes will note every error in diagnosis, every failure in results of treatment. Moreover, the very act of teaching clarifies and crystallizes his own knowledge; in attempting to explain, the dark places become prominent and demand investigation, and hence it is that those cases which are lectured on receive the best treatment. I need say nothing here on the other side of the question, the value of properly trained physicians to the community and the necessity for hospital instruction in such training; Johns Hopkins understood all this and specially directed that "in all your arrangements in relation to this hospital you will bear constantly in mind that it is my wish and purpose that the institution shall ultimately form a part of the Medical School of the University."

Now there are medical schools and medical schools, and in obeying this direction of the donor the trustees had to consider what sort of a medical school this school of the university was likely to be. As the majority of the trustees were also trustees of the university, they knew well the principles which underlie the organization of that institution, and that the same principles would govern the organization of the medical department when that came to be taken in hand. One of these principles is the thorough teaching of that which is known, another is to increase that which is known, and to furnish the men

and means for doing this. So also the hospital should not only teach the best methods of caring for the sick now known, but aim to increase knowledge, and thus benefit the whole world by its diffusion. Another point which had to be kept in view was the direction of Mr. Hopkins that there should be established, "in connection with the hospital, a training school for female nurses, not only to care for the sick in the hospital, but to benefit the whole community by supplying it with a class of trained and experienced nurses."

It is also highly desirable that a hospital of this kind should have connected with it a well-appointed dispensary for the treatment of those who need medical aid, but not a bed, in the hospital. Through such a dispensary much good can be done at small cost, the selection of proper patients for the hospital is facilitated, the means of medical investigation and teaching are greatly extended, and the scope of the nursing system can be made to reach the poor and ignorant in their own homes.

The last point to which I shall refer, which was kept in view by the trustees in deciding upon the plans, was the general appearance of the buildings and grounds.

Mr. Hopkins gave no specific directions as to the buildings, but he directed that the grounds should be properly enclosed by iron railings, and so laid out and planted as to be a solace to the sick and an ornament to the city, and it was evident that the buildings should be of the same character so far as their purpose would admit. It was therefore decided that, while no utility should be sacrificed for the sake of architectural ornament, and the main purpose which I have referred to should be fully worked out in the plans before any attention was paid to external appearance, it was fit and proper that the buildings should form an ornament to the city, and a suitable monument to the memory of the donor.

Bearing in mind, then, these main principles, to provide for the proper care of the sick, both rich and poor, to provide for the highest class of medical education, to increase and diffuse knowledge, to provide trained nurses for both hospital and city, to provide a dispensary, and to make the buildings and grounds ornamental and attractive, let us see how the problem has been thus far worked out.

I will begin with the arrangements for securing that article of prime

necessity in a hospital, viz., pure air. Air supply and ventilation in this climate are inseparably connected with heating for a considerable portion of the year, for comfortable warmth must be secured, and on the means of doing this must largely depend the methods of ventilation and their success. The temperature of Baltimore may vary from 103° in the shade to 17° below zero F., hence its perfect hospital must be one which would answer for the tropics or for northern Russia. To secure this, double walls, with air spaces, were given to the buildings, and a system of heating by the circulation of hot water was adopted for the wards. This system consists of central boilers, from which flow and return pipes extending beneath every building, connected with heating coils, of which there is one for every two beds in the ward above. The temperature in these coils can be exactly regulated to any temperature between 150°F. and the temperature of the external air by simply regulating the velocity of the flow of water by the valves attached to each coil, and thus it is quite possible to give one pair of beds a temperature of 70° and another pair in the same room, at a little distance, a temperature of 60°F., to suit the needs of different cases. The 80,000 gallons of water contained in this heating apparatus go round and round, carrying heat from the furnaces to the wards; but every building has its own independent means of ventilation, and it is not possible to go from one ward into another without going into the open air on the way, so that foul air, if any forms, cannot spread from one building to another. Nevertheless, the buildings are so connected by corridors and underground tunnels that in passing from one to another there is no exposure to rain or snow, and the least possible to cold air, while the food is not exposed at all. This is not the place to describe the ventilation. I will only call your attention to the fact that the temperature of the incoming air by any bed is easily changed by turning a valve, while the quantity of air is not changed; to the arrangement for taking foul air from either the bottom or top of the ward, or from both, and to the fact that all this has been thoroughly tested during two winters and found to give the results hoped for.

One of the peculiarities of the wards is that all the service rooms are collected at the north end, leaving the south end free of obstruction and fully exposed to the sun, the end of the ward being a large bay

window looking out on the central garden, and with a floor which can be warmed so that the patients, able to sit there, can be thoroughly comfortable. Another peculiarity of the sick wards is the arrangements for easy cleansing, and to prevent possible accumulations of dust in corners and crevices. Corners are to a great extent done away with, and easy curves given in their place; even at the junction of the floor and walls there is a curve instead of the usual right angle, and I advise you to look at it and see how it has been produced, for it ought to become fashionable, and take the place of the old mop-board in all well-constructed houses. So, also, the doors have not the usual moulding about the panels, giving recesses which it is almost impossible to clean.

One of the wards is especially arranged for cases which may be either contagious or offensive. In this building each patient is in a room by himself, and all these rooms open into a corridor through which the wind is always blowing. There are many details about this isolating ward which are worth looking at, but which I have not time now to refer to, and I must omit details about the pay ward, the octagon ward, and the peculiar fittings and conveniences of the kitchen, laundry, apothecaries' building, etc., for the same reason.

Let us pass now to the second object of the hospital, the giving means for higher medical education, and see what has been done for that. In the first place, there is a large amphitheatre with appended rooms for the reception of accidents and emergencies of all kinds. In the second place, provision is made for at least thirty students to reside constantly in the hospital and devote themselves under proper guidance to the study of disease and the practical care of the sick. It is intended that these places shall be open only to those who have had a thorough previous training, and who have shown themselves to be fitted to undertake this important part of their studies. As a rule, not more than five per cent of medical graduates have had any opportunities worth speaking of to study and treat diseases in the living man when they receive their diplomas. They have to get this experience on their first patients, and sometimes the experience is rather hard—for both doctor and patient. This hospital has provided for the class of the medical school in the last year of their studies good rooms with bath-rooms, a dining-room, and other conveniences, and here they

can be taught the actual daily work of a physician, for which all their previous studies are only preparatory. Many of the arrangements of the hospital have been constructed with reference to this instruction; it is a great laboratory for teaching the practical applications of the laws of hygiene to heating, ventilation, house-drainage, and other sanitary matters. All pipes and traps are either exposed to view or can be seen by merely opening a door, and in the tunnel beneath the corridor you can study at your leisure the complicated and yet simple arrangement of pipes for gas, steam, water, sewage, etc., which are usually buried and remain a profound mystery to every one except the plumber, and often puzzle even him.

Closely connected with this subject of teaching is that of increasing our knowledge of the causes, symptoms, results, and treatment of disease; in fact one cannot be thoroughly and well done without the other, and hence many of the provisions for the one are also useful for the other. For example, to go back to our system of heating and ventilation, there are many points connected with it which are destined for experimental work, to compare steam with hot-water heating, to determine the velocity of water at different temperatures, to compare ventilation by aspiration with that by propulsion, or by upward currents with those drawn downward.

One structure is very largely devoted to and fitted for experimental research, and that is the pathological laboratory, where the causes, processes, and results of disease are to be studied. Upon the results obtained in that laboratory may yet depend the saving of many lives, the relief of unspeakable agony, the warding off of pestilence from the city, and, to put it in a strictly business light, the value of real estate and the rate of taxation of this community. We are on the verge of great advances in our knowledge of the causes and methods of disease, and I feel sure that these will be only preliminary steps to far greater and better knowledge of how to prevent or to treat them than we now have. The probable length of life of the new-born infant to-day is not much more than half what it ought to be; the practical productive period of the life of our men and women is shortened and interrupted by unnecessary disease and suffering; but remember, if these things are to be amended, it is not merely by teaching old doctrines; we must open fresh windows and let in more light, so that we can see what these

obstacles really are. It is in this work of discovery that it is hoped that this hospital will join hands with the university, and it is in this hope that some of the structures around you have been planned and provided.

A word now on the fourth object kept in view in this hospital, viz., the training school for nurses.

Some of you probably have had some personal experience of the difference between an educated, properly trained female nurse, and one of the old-fashioned sort, but if you have not, it would take much more time than I now have to describe it. I can only say that in many cases a competent trained nurse is as important to the success of treatment as a competent doctor, and that one of the greatest difficulties in treating well-to-do patients in their own homes in this city is the want of proper nurses. Affection and zeal may do much, but they cannot take the place of knowledge, and this kind of knowledge is not to be acquired in a day or in a month. It is a work best carried out by women, though not one woman in ten is fit for it, or should undertake it. But the woman who is fit for it, who has physical health and strength, sound sense, loving kindness, patience and tact, and who has been thoroughly taught the art of nursing the sick, with all its thousand details, has the power of doing good and increasing happiness to a degree which few others possess. In a properly conducted hospital ward she is a necessity, but her field of usefulness and helpfulness is by no means limited to that. She is needed outside the hospital, in the home of the rich to nurse and care for the sick; in the home of the poor, to teach prevention as well as nursing. To gather here such women, to have them thoroughly instructed, to furnish them with the attractive and comfortable home which they deserve, and to send them where they are most needed, with provision for their return when the work is done, is the object of the training school of this hospital.

For this purpose the trustees have provided a large and handsome building, separated from the others, and exclusively appropriated to the female nurses, where each can have her own comfortable room, and where a common parlor, library, dining-room, bath-rooms, and, in short, the arrangements of a first-class hotel are provided for their use. Here also is a training-kitchen and a lecture-room to aid in the

work of instruction. The intention is that when the nurse has finished her six or eight hours' tour of duty with the sick, she shall come quite away from the ward and all that pertains to it, and take her rest and recreation in a totally different atmosphere, and special effort has been made to have this home attractive and pleasant.

The fifth object which I mentioned as having been kept in view in the plan and construction of these buildings is the dispensary. This is a large building on the north front, consisting of a large central waiting-room, surrounded by a number of smaller rooms for the use of the physicians and surgeons who are to examine and prescribe for the patients, and having bath-rooms, and a small apothecaries' establishment for the issue of the medicines ordered. This building is connected with the amphitheatre by a short covered corridor, and is specially arranged with reference to teaching. It, as well as the amphitheatre, is heated by steam instead of hot water, partly because they are not in constant use, and a rapid means of warming is desired, partly for the purpose already referred to of giving the means of experimental comparison of the two systems. The means of supply of fresh warm air in these two buildings, and of removing the air made impure by exhalations, are somewhat peculiar, and merit examination.

With regard to the architectural design and external appearance of the buildings, and the laying out and ornamentation of the grounds, I can only say that you must see and judge for yourselves whether Mr. Hopkins's wish that they should be an ornament to the city has been successfully complied with. So far as external ornamentation is concerned, it is confined almost entirely to the large buildings on the west, or Broadway, front, which it was felt should harmonize in style of decoration. These central buildings, consisting of the administration, with the one pay ward on either side, are constructed of pressed brick with ornamentation of a dark blue, fine-grained, hard, and durable stone, known as Cheat River stone, and of molded terra-cotta of the color of the brick. The external designs for these, as for all the other buildings, were furnished by Messrs. Cabot and Chandler, of Boston, and I think we have good reason to be well satisfied with the results they have produced. The grounds are laid out and planted in accordance with designs furnished by Mr. E. W. Bowditch, of Boston.

As regards construction, I do not hesitate to affirm that these are the best built buildings of their kind in the world. The material is the best, the most skilled and careful workmen were employed, and, above all, the work received the most careful, conscientious, and intelligent supervision as it progressed. For this supervision we are indebted to Mr. John Marshall in the beginning and to Mr. William H. Leeke for the remainder and conclusion of the work; and we are also indebted to the latter for many valuable suggestions as to modes and details of finish which are so important in a hospital. The details of the complicated and extended system of heating, ventilation, and plumbing were designed and the work executed by Messrs. Bartlett, Hayward & Co., of this city. I should like to go on and mention the names of a number of other persons who have done good work here, but want of time forbids. I will only say that these buildings embody the counsels and suggestions of many men and women in this country and abroad, but among them all there is no one who, from the very beginning of the conception of the idea of this magnificent gift in the mind of Johns Hopkins down to this present moment, has had more to do with shaping the results, who has furnished more valuable suggestions, who is more thoroughly acquainted with all that has been done and why it has been done, who has worked so unselfishly, and who more deserves honor in this connection than the president of the board and chairman of the building committee through the whole progress of the work, Mr. Francis T. King.

Briefly and incompletely as I have sketched these salient points of the plans and purposes of this hospital, I hope I have, nevertheless, shown you that it is intended for other purposes besides providing shelter, food, and drugs for the sick. In saying this I have not the least wish to undervalue or disparage those institutions which do make this their main or only object. There is abundant need of their existence and work also; but this institution should not be judged by the rules which apply to them; it cannot be managed after their fashion; if it does not produce results different from theirs it is a failure and the expenditure upon it a mistake.

Thus far I have been speaking of the buildings only, and trying to give you some idea of the motives which led to their being as they are, and what they are, and not otherwise. From the beginning, however,

it has been recognized that the buildings and machinery are only means to an end, tools which must be handled by skilled workmen to produce the desired result; and throughout all these years of planning and building the question of organization and of the sort of men and women who were to use and work with these things has not been lost sight of. It is true that no attempts were made to select and engage individual members of the hospital staff until quite recently; but there was, nevertheless, a tolerably definite conception as to the ideas, mode of work, character, and wants of those who are to constitute this staff, and when the time came for selecting, it was made by this standard.

On the philanthropic, social, and religious aspects of this great trust I do not propose to touch, but I wish to say a very few words of the hopes and wishes of scientific men and physicians with regard to it. From the time of the first announcement of the Hopkins bequests to the present, these men, all over the world, have been keenly interested in the plans and methods adopted in carrying them out. Whenever and wherever the problems of higher medical education have been discussed within the last ten years, there has been speculation as to the probable course of the Johns Hopkins medical department, and the influence it would have upon the standard. I may even say that some of this influence has been exerted in advance, has been discounted, as it were, for the plans of this hospital have stimulated changes in some of our best medical schools, and have been copied with more or less modification in some of our latest hospitals.

What is it, then, that the physicians want? Is it more physicians, more family practitioners, more surgeons, more specialists? Not at all. They know very well that there is no danger that the supply will not be equal to the demand; when they become overburdened with practice they do not at present find it difficult to obtain assistants; they have no fear lest the seventy or eighty medical schools of this country should fail to produce a sufficient number of medical practitioners to meet the wants of our increasing population; and they know also that the medical schools of Great Britain and Germany are sending to us quite as much of their product as we can conveniently dispose of. They hope that the Hopkins medical school and hospital will do two things. The first is, that it will demand of those who

propose to become its students evidence that they have a sound basis of preliminary education before they commence, and that its standard in this respect shall be little below that of the requirements for granting the degree of bachelor of arts in the university. It is hoped that the men thus selected will go through a carefully graded course of study, including actual work in properly fitted laboratories, and that after this they will be brought into contact with the sick, and thus obtain practical experience of the duties and responsibilities of the practitioner of medicine before they offer their services as such to the public.

So much our physicians desire of every medical school, for the sake of the honor and dignity of the profession, and for the good of the public, and they desire especially that this school shall form an example to which they can point as showing how medical education should be conducted, and what should be required of the candidate for the degree of doctor of medicine.

The very general interest in the combined Hopkins trusts felt by physicians and scientific men not only of this country but of the whole civilized world, is largely due to the belief that the relations which will here exist and be maintained between the university as a whole and its medical department, of which this hospital is to be an important part, will be close and intimate, so that the true university spirit will pervade, stimulate, and encourage the hospital work. In this country medical schools have either had no connection with universities properly so-called, or the connection has been slight and nominal, such as depends upon the formal conferring of medical degrees by the university. Here, however, through the influence of the biological department, there are secured common interests and mutual influence, and it is hoped therefore, that the necessary details of technological instruction will be arranged in accordance with and subordinate to the broad principles of scientific culture upon which this university is organized.

It is because it is believed that this will be the case that there is a widespread hope and expectation that these combined institutions will endeavor to produce investigators as well as practitioners, to give to the world men who can not only sail by the old charts, but who can make new and better ones for the use of others. This can only be done where the professors and teachers are themselves seeking to

increase knowledge, and doing this for the sake of the knowledge itself;—and hence it is supposed that from this hospital will issue papers and reports giving accounts of advances in, and of new methods of acquiring knowledge, obtained in its wards and laboratories, and that thus all scientific men and all physicians shall share in the benefits of the work actually done within these walls. But, however interesting and valuable this work may be in itself, it is of secondary importance to the future of science and medicine, and to the world at large, in comparison with the production of trained investigators, full of enthusiasm, and imbued with the spirit of scientific research, who will spread the influence of such training far and wide. It is to young men thus fitted for the work that we look for the solution of some of the myriad problems which now confront the biologist and the physician.

Do I seem to ask too much? to be too sanguine as to what human thought, and study, and skill may accomplish? to forget that there is one event unto all; that the shadow of pain and death comes on the wise man as on the fool? I have two answers. As surely as our improved methods of prevention and treatment, based on the advances in knowledge of the last fifty years, have already extended the average duration of life in civilized countries nearly five years, have prolonged thousands of useful and productive lives, and have done away with the indescribable agonies of the pre-anæsthetic period, so surely we are on the verge of still greater advances, especially in the prevention of infectious and contagious disease, in the resources of surgery against deformities and morbid growths, and in the mitigation of suffering due to causes which cannot be wholly removed. But the second answer is more important, and it is this: It is our duty to try to increase and diffuse knowledge according to the means and opportunities which we have, and not to rest idle because we cannot certainly foresee that we shall reap where we have strewn. "It is not incumbent on thee to finish the work, but thou must not therefore depart from it," says the Talmud, and "Of him to whom much is given much shall be required," says the Scripture.

To you, the officers of this institution, and to you, men and women of Baltimore, there is now given the opportunity of giving powerful aid in this increase and diffusion of knowledge of the laws of human

life, disease, and death. Surely, those who are working in the wards and laboratories of the hospital and university will do their best; surely, also, the citizens of this great city, of a great nation, which at no distant day will take the lead in scientific work, will encourage, sustain and sympathize with these workers. I would have this hospital become famous, not for fame's sake, but because this will be evidence of the good work which has been done in it; but we must not be impatient. There are difficulties to be overcome, delays which must be submitted to. We cannot at once have the medical school which is essential to the plan which I have sketched; but there is plenty to do for the present, and I am certain that in time all these present obstacles to full development will be happily overcome.

Success in this, as in all other enterprises in this world, is to be obtained by unselfish work for the good of others, by wise counsel, by coöperation, and by persistent effort.

A hospital is a living organism, made up of many different parts, having different functions, but all these must be in due proportion and relation to each other, and to the environment, to produce the desired general results. The stream of life which runs through it is incessantly changing; patients and nurses and doctors come and go; to-day it has to deal with the results of an epidemic, to-morrow with those of an explosion or a fire; the reputation of its physicians or surgeons attracts those suffering from a particular form of disease, and as the one changes so do the others. Its work is never done; its equipment is never complete; it is always in need of new means of diagnosis, of new instruments and medicines; it is to try all things and hold fast to that which is good.

"Et quoniam variant morbi, variabimus artes."

It has been said that "hospitals are in some sort the measure of the civilization of a people", but a hospital of this kind should be more than an index. It should be an active force in the community in which it is placed. When the mediæval priest established in each great city in France a Hôtel Dieu, a place for God's hospitality, it was in the interests of charity as he understood it, including both the helping of the sick poor and the affording to those who were neither sick nor poor an opportunity and a stimulus to help their fellow-men; and doubtless

the cause of humanity and religion was advanced more by the effect on the givers than on the receivers. It is the old lesson so often expounded, apparently so simple and yet so hard to learn, that true happiness lies in helping others; that it is more blessed to give than to receive.

In some respects we to-day have a much wider outlook than the men of a thousand years ago. This hospital is designed, as I have told you, to advance medical science as well as to give relief to the sick poor, but the fundamental motive is the same—to help others.

We have here the beginning of an institution which shall endure long after the speakers and the audience of to-day shall have finished their lifework and have passed away. Founded in the interest of suffering humanity, intimately connected with a great university, amply provided with what is at present known to be essential to its work, we have every reason to predict for it a long and prosperous career, with steadily progressing improvement in its organization and methods, and enlargement of its activity and influence.

Let us hope that before the last sands have run out from beneath the feet of the years of the nineteenth century it will have become a model of its kind, and that upon the centennial of its anniversary it will be a hospital which shall still compare favorably, not only in structure and arrangement, but also in results achieved, with any other institution of like character in existence.

CHARITY AND KNOWLEDGE*

DANIEL C. GILMAN

Thirteen years ago during the centennial celebrations of Independence Day, the University founded by Johns Hopkins began its work, and now, as we commemorate a completed century of constitutional life, the Hospital, gift of the same donor, throws open its doors. These buildings—on which thought, time and wealth have been freely spent—are now consecrated to the ministry of mercy and the prolongation of life. Science and charity, knowledge and pity, skill and sympathy are here installed in the service of mankind.

That large-minded citizen of Maryland, "who by noble gifts for the advancement of learning and the relief of suffering, has won the gratitude of his city and his country," found two words adequate to his great ideas. "University" and "Hospital" were his chosen terms, and he linked them together by this significant phrase: "Bear constantly in mind that it is my wish and purpose that the hospital shall ultimately form a part of the medical school of that university for which I have made ample provision by my will." How brief the phrase, how large the purpose! "Apples of gold in pictures of silver."

Like James Henry Roosevelt of New York, "a man upright in his aims, simple in his life and sublime in his benefaction,"[1] whose hospital and dispensary give clinical instruction to the College of Physicians and Surgeons; like James Lenox of New York, whose munificence established a public library and gave birth to a hospital, Johns Hopkins, already honored as a patron of learning, will be henceforward remembered in the annals of charity and medicine. May we not almost say of him as Pindar said of Theron.

* From *Johns Hopkins Hospital: Addresses at the Opening of the Hospital.* Privately printed. Baltimore, 1889.

The footnotes in this address were added by the speaker, not by the Editors.

[1] This phrase (like that above, referring to Johns Hopkins) is taken from a memorial tablet.

—and I will swear
That city none,—tho' she unroll,
A century past, her radiant scroll,—
Hath brought a mortal man to light
Whose hand with larger bounty flows.
The blessings to that man we owe
Say who shall hope to count.[2]

We may form an idea of what this hospital may become by the study of a like institution in London. About a century and a half before Johns Hopkins died, the days of Thomas Guy were ended. Like our benefactor, he had lived unmarried to the age of eighty years, and from humble beginnings had acquired a fortune, with which he provided for the establishment of a hospital. The amount of his gift was more than a million of dollars (£238,292). The beneficent influences of Guy's hospital are now known in every part of the globe. It is doubtless safe to say that every one of us has shared, indirectly, in its benefits. The name of the great surgeon, Sir Astley Cooper, would alone give renown to the hospital to which he was attached,—Sir Astley Cooper, of whom it was said that from the period of his appointment to Guy's, until the moment of his latest breath, he was everything and all to the suffering and afflicted; his name was a host; but his presence brought confidence and comfort.[3] Addison and Hodgkin, whose names are familiar to the historians of medicine, were physicians in that hospital. So was Richard Bright whose discoveries have been pronounced the most important contribution to medical science, made in the first half of the nineteenth century. The observations and studies made in Guy's Hospital since 1836 fill fifty volumes. Thousands of medical students have been trained within its walls; "their presence," says a competent observer, "has made the hospital." Hundreds of thousands of patients have received relief from the treatment there afforded. In a single year, five thousand in-door patients have been cared for and more than thirty thousand out-door patients have sought advice.

But we are planning for a future much longer than a century and a half; for a history as long as that of St. Bartholomew's or St. Thomas's, which now, after many centuries, are more useful than ever.

[2] Olympic II, Cary's version.
[3] Letter of Dr. Roots in the Memoir of Sir A. Cooper.

By a curious coincidence, as I had reached this point in the preparation of my address, I received a volume from Dr. Norman Moore, the Warden of St. Bartholomew's Hospital in London—bearing an inscription so welcome and so apposite that I will read it. "To the library of the newest of Hospitals this account of the progress of medicine in one of the most ancient is given by Norman Moore, with the earnest hope that the Johns Hopkins Hospital may flourish at least as long as the Royal Hospital of St. Bartholomew, in Smithfield, and prove no less useful to mankind,—on the opening day of the Johns Hopkins Hospital, 1889."

This little book is full of suggestions for us. First, as to the longevity of a hospital. "For more than seven hundred and fifty years the hospital has flourished upon its present site, and its Smithfield gateway, through which passed men of the generation whose fathers saw William the Conqueror enter London, has ever since been open to the sick poor."

Then as to the progress of medical science. Here you may see "how the physician grew from a schoolman into a scientific observer, and how the surgeon, who appeared on the scene in livery and without learning, grew from a handicraftsman to be a man of science."

Next as to the training of illustrious men. Here you will find a record of the names and services of Caius, Bernard, Pott, Abernethy, Lawrence and Paget; you may learn that Dr. Thomas Young, the originator of the undulatory theory of light, was here a student, and you will come upon the story of one more famous than any person I have named, the discoverer of the circulation of the blood, the illustrious Harvey.[4]

Time may efface the personality of our founder, as it has effaced the personality of Rahere, the founder of St. Bartholomew's, but the beneficence of Johns Hopkins will last for centuries; and gratitude will cherish the memory of his broad views, his great liberality, his wise and beneficent purposes.

The previous speakers have told us of the circumstances which led to the construction of these buildings and have described their pur-

[4] Dr. Moore calls attention to the fact that it was a fund given by Dr. Caius to encourage the study of anatomy, which was the immediate means of leading Harvey to his discovery, and also to a remark in one of Harvey's lectures that it was a passage of Aristotle which first suggested to him the idea.

poses. Let me from a different point of view point out some of the benefits which are likely to proceed from this foundation. As I enter upon this theme, I am reminded that in 1789, John Howard, *facile princeps* among modern philanthropists, published in a quarto volume, just before his death, the observations he had made upon the Lazarettos of Europe. That was the beginning of reforms in prisons, asylums, refuges, and hospitals. To this work he prefixed these words of Cicero, a motto so appropriate that I might take it for a text: *Quid tam porro regium, tam liberale, tam munificum, quam opem ferre supplicibus, excitare adflictos, dare salutem, liberare periculis.*[5]

First, last and always, this hospital is to furnish relief to the sick and wounded. Make the best of it, introduce fresh air and sunshine, and provide the utmost comfort, secure wise physicians, engage the best trained nurses, decorate the walls with pictures, bring fruit and flowers and books and friends,—and even the comforting influences of Religion, yet you cannot conceal the direful consciousness, that this is the home of suffering.

> From any other ill,
> (Except it be remorse) can men escape
> By work,—the healing of divinest balm
> To whomso hath the courage to begin:—
> But sickness holds the sick man in a chain
> No will can break or bend to earthly use.[6]

The names that have been given to these abodes of the sick are suggestive. Hospitality and hospital alike suggest the bestowal of kindness to guests. The word Lazaretto, ultimately degraded, pointed at first to the restoration of life. Misericordia, *la Charité*, *la Pitié*, the Home of the Good Samaritan, the House of Mercy, bring to mind the kindly influences of love and care. St. John, St. Thomas, St. Bartholomew and St. Luke, above all other apostles, are favorite patronymics. Paracelsus died in the Hospital of St. Sebastian. Bethlehem, Bethany, Bethesda and Jerusalem recall the scenes where the Great Physician was present. The name of Christ has been given to many a foundation. In other places the hospital shares with the temple the name of Hôtel-Dieu or House of God.

[5] Cicero, *De Oratore*, I. 8.
[6] Ugo Bassi's "Sermon in the Hospital," p. 13.

By whatever name it may be called this is a convent where sickness is the abbess. The rule of sympathy for the suffering must govern every body with a strictness of discipline as rigid as the rule of the Benedictines or the Carthusians. Those who daily walk these cloisters will be the warders of life and health, however high their station or however humble their service; and casual visitors will not cross the threshold of the wards without pity for those who are disabled or without admiration and gratitude for those whose lives are spent in alleviating distress.

This hospital will not only meet the daily calls of humanity, it will stand ready to render extraordinary services in those emergencies which not even the progress of municipal reform and preventive medicine can entirely ward off. A fire, an explosion, an accident on the rails or on the sea-shore, the fall of a platform or of a building poorly constructed, may at any moment tax the utmost resources of a great establishment. True, we have no fear of leprosy and the plague; we have almost ceased to dread the coming of the cholera; yellow fever, we are hoping to thwart in its approaches to our northern seaports;—vaccination, which was spoken of by Sir James Simpson, "as the greatest thought ever broached in practical medicine" is a great prophylactic; but we are not certain that diphtheria and infectious fevers will not continue to be epidemic; nor can we always be sure that the boards of health in the city and State will succeed in protecting us, as well as they can, from the inroads of pestilence. Indeed it is well to inquire whether Baltimore is now fortified as it should be against the hostile incursions of epidemic disease. In addition to its other functions, this hospital will stand as a reserved force, a sort of storehouse of energy, ready to serve the city if apprehension and disease spread their pall upon it.

Here let me say, in anticipation of the future, and in memory of the past, that in all the records of bravery on land and sea none are more noble than those of the medical profession. Free from all excitement, free from the hope of reward, free from any commands but those which are divine, they have in times of pestilence gone from bed to bed firm, fearless, faithful, carrying the offerings of cheer, comfort and relief, and often of restoration to health and vigor. For them, there is no repose in time of danger. The black wings of death hovering

over a city do not deter them from duty; and often it may be said of them as Milton said of Abdiel, "faithful found among the faithless," faithful only they. Read the annals of modern pestilence, of cholera in New York, of fever and famine in Ireland, of yellow fever in the South. Every where it is the same story. The more direful the record, the more unflinching, the more self-forgetful, the more humane are the efforts of physicians.

While the offices of a hospital are bestowed without money and without price on those who are destitute,—those who are able to pay for suitable attendance, and for the domestic comforts to which they are accumstomed, may discover that they can here be better treated than in many private houses. The conditions of quiet are more easily secured; suitable diet at unusual hours can be commanded; medical attendance is within call at every moment of the day and night; manifold appliances for relief are more readily obtained. More and more frequently, travellers, students, all whose homes are in hotels and boarding houses, and even many who have good private homes, turn toward good hospitals when they see the need approaching for prolonged and special care. For the wants of such persons provision has been made in the wards here set apart for paying patients,—male and female.

This hospital would be a very narrow institution if it kept to itself its experience. It is the essence of quackery to deal in mysteries and nostrums; it is the glory of medicine that it owns no patents and conceals no discoveries. On the contrary, the best hospitals of the world consider it one of their first duties—second only to the care of their patients—to record the cases they have treated, the methods they have pursued, the results whether favorable or unfavorable which have followed. Scientific studies in pathology and practical medicine must be printed. Special papers, often requiring costly illustrations, must be published upon extraordinary cases, and upon new operations and modes of relief. It is thus that the science of Medicine is advanced. Where secrecy reigns, carelessness and ignorance delight to hide; skill loves the light.

It is impossible to have a hospital without its becoming a place for medical education. It is interesting to note that in the physician's oath, attributed to Hippocrates, the duty of imparting knowledge is explicitly enforced. Even the country doctor as he rides from village

to village, takes in his gig an observing pupil, like the squire to a knight-errant. Every great surgeon is watched with the closest attention by the younger physicians who assist him. Every mother is the pupil of the physician whom she calls upon to attend her suffering child. So, of course, a hospital, having upon its staff men of rare qualifications who are in daily consultation with their most skilful brethren, is, from the necessities of the case, a place for instruction. How systematic that instruction will be depends on circumstances that at the moment need not be presented. All that need now be said is that hospitals the wide world over are the schools of medicine and surgery.

The training of nurses is another form of hospital activity, recently developed, never hence to be abandoned. To the sisterhoods of the Roman Catholic Church, to the Protestant Deaconesses of Kaiserswerth and the Bethanien at Berlin, and to many guilds in many lands, much credit is due for lessons they have taught the world, as to the importance of training nurses. Elizabeth Fry was one of the first Englishwomen to propose such instruction. Florence Nightingale, by her services in the Crimean war, and by her subsequent writings, has borne a noble part in this work. So, too, have our own countrywomen. The civil war, full of sad recollections, has some bright stories, and among them none more inspiring than the labors of brave, self-sacrificing and intelligent women in the Hospitals. Who that has read "What we did at Gettysburg," or "Hospital Days," has forgotten their lessons? As a direct result of the war, Nurses' Schools have grown up in every part of this land. Our Hospital has such a department soon to be opened, where nurses will be trained, not only for their merciful offices within these walls but for household engagements and for visiting among the poor.

A good hospital may readily become the rallying place of the medical profession who are resident in the City.

> "Through mutual intercourse and mutual aid
> Great deeds are done and great discoveries made;
> The wise new wisdom on the wise bestow
> Whilst the lone thinker's thoughts come slight and slow."

One purpose of this central building is to afford opportunities for professional intercourse. Here are rooms set apart for the library

that will presently be collected; here the medical journals will be taken in; here are the best appliances and instruments for the treatment of patients; here are rooms for private consultations and for public conferences; here are laboratories for physiological and pathological determinations; and it will not surprise me to hear that within a very short time medical associations are here brought together "for mutual intercourse and mutual aid" at the invitation of Dr. Osler, the physician in chief, who this day assumes his great responsibility with the hearty welcome of Baltimoreans, and with the well-earned confidence of the profession throughout the entire land.

Reference must also be made to the lessons that this hospital has already given to the world, before a single patient has been received. The vast amount of thought bestowed upon these buildings, not only in their general arrangements,—but in thousands of details which promote their efficiency, has not failed to attract the attention of observers from every part of the globe. The letters which have been received during the last few days from the most distinguished surgeons and physicians abroad, and the presence of this large body of medical men from the distant cities of the United States are indications of this interest.

Finally, if this hospital becomes the seat of knowledge in all that pertains to the nature of disease, its treatment, its prevention and its cure, it will of necessity be a constant guide to the people of the city and the State in which it is placed; it will promote the general health of the inhabitants. There is an altar in one of the churches of Messina, which bears an inscription to Aesculapius and Hygeia, the God of Medicine and the Goddess of Health; and their statues are found together on the facade of Guy's Hospital. May they always be associated in Baltimore.

Is all this outlay wise? I might answer an inquirer in the words which Wordsworth employed in speaking of King's Chapel, one of the most costly structures in the University of Cambridge.

> "High heaven rejects the lore
> Of nicely calculated less or more,
> Tax not the royal saint with vain expense;
> With ill-matched aims, the architect who planned
> This glorious work of fine intelligence."

For in this hospital, as in that church, are

> "Thoughts whose very sweetness yieldeth proof
> That they were born for immortality."

But I prefer to give a more specific and appropriate reply to those (if any such there be) who say, "I believe in everything that is practical, in whatever leads to the relief of suffering; but I am afraid of this talk about science. I would rather see a thousand beds for patients than any provision for medical education." Such reflections are to be heard with respect, for they are natural to minds unacquainted with the intimate relations which subsist between the progress of medical knowledge and the progress of medical art. Nevertheless it is true that those who have most carefully studied the conditions by which human life is perpetuated, human sufferings lessened and human vigor increased, are well aware that every step forward in science leads to many forward steps in practice. May I endeavor to be a mediator between these two divergent views and bring a few illustrations from the Doctor's shop to the attention of those who are practically interested in hospitals, but who have paid no attention to the steps, so slow, so difficult, so uncertain at first but so sure at last, by which the Healing Art makes progress.

The late Dr. Austin Flint of New York in an address prepared near the close of his life, has pointed out with the wisdom of experience the probable "Future of Medicine." It would be presumptuous for me to attempt to do again what he has done so recently and so well. But on this day of promise, in view of all this expenditure, it is fitting that we should bring to mind some inspiring thoughts.

Let us first consider the benefits which have come to mankind from the opportunities which hospitals have afforded for the observation of disease. There is no one among us more competent to speak upon this subject than the pathologist of this hospital, Dr. William H. Welch, who, years in advance of its opening, has been engaged as a professor of the university in the study of the nature and origin of disease. He has called my attention to these noteworthy points:

"Those who have contributed the most to the advancement of practical medicine and surgery have accumulated their experience largely in hospital service. By the constant attendance of skilful

physicians and of well-trained nurses in hospitals, precise observations can be made and the phenomena of disease and the influence of treatment determined under the most favorable conditions.

"Our present knowledge of the natural history of disease, of its diagnosis, prognosis and treatment are based to a very large extent upon experience derived from hospitals. Text books, monographs and medical journals incorporate this experience and bring it to the knowledge of the medical profession. This is why intelligent physicians are always eager to secure the advantages of a hospital service."

The benefits which medicine has received from purely scientific investigations may be shown by so many examples that it is difficult to make a selection among them. Dr. Welch mentions these:

"Upon the foundation laid by Helmholtz's researches in physiological optics, and his discovery of the ophthalmoscope, the art and science of ophthalmology have developed into the most accurate department of clinical medicine.

"The investigations which received their impulse from Du-Bois Reymond in the difficult subject of animal electricity have rendered electricity available for diagnosis and treatment, and have advanced thereby our knowledge of nervous diseases.

"Of the many ways in which the work of the chemist has aided medicine may be cited, as one of its most recent contributions, the introduction into modern therapeutics of many useful remedies which are the products of synthetic chemistry. Doubtless this is a field which will be cultivated still further, and it would be rash to attempt to foretell what agents for the cure of disease and relief of suffering are still hidden in the chemist's laboratory.

"By the discovery of the specific germs causing various infectious diseases, surgical practice has been revolutionized. It has become possible to prevent the infection of wounds from the exterior, and thus to guard against a host of traumatic infections which rendered dangerous and futile so many surgical operations. Preventive medicine has taken its place among the exact sciences.

"Accurate knowledge of the causes of disease now forms a sure basis for intelligent therapeutics and there is every reason to expect that the future will bring to light means to overcome the injurious agents which are now, for the first time, known."

But there is another illustration so marvelous that it may almost be called miraculous. The relations of advancing knowledge to advancing charity are brilliantly displayed by the history of methods for the relief of pain.

To put a stop to suffering is an instinct of human nature, distinguishing man from animals. The most scientific men, and the most practical are agreed upon this, and have been so agreed for centuries. But Anaesthesia, most welcome of all the angels of mercy, came down from heaven. When the older surgeons in this assembly were students, opium and alcohol were the imperfect anaesthetics most usually employed. Their use was restricted and unsatisfactory if not dangerous. No one can tell what was suffered in places where gentle sleep now quiets apprehension and makes the patient unconscious of his state. To this alleviation, we are so wonted that we accept it as the air we breathe. But if you would learn how man secured this boon, how many efforts of scientific and of practical men were combined before the results were reached, recur to the history of four modern agencies, nitrous oxide, ether, chloroform, and cocaine, which are like "the gentle dew from heaven, which blesseth him that gives and him that takes." It is a chapter more wonderful than any romance of the Arabian Nights.

Let any one present who is skeptical in respect to the usefulness of science to the healing art, keep this record in his mind. Let him reflect on the apprehensions that have been removed not only from the patient but from his attendant friends; let him see how much easier and therefore how much more certain the task of the surgeon has been made; and above all let him think of the hours of pain that have been absolutely annulled, and then let him divide the honors if he can, which belong to Science from those which belong to Philanthropy; let him balance half a century of scientific relief with the previous practice of many thousand years; then let him tell us which is better.

From the past let us turn to the future. All the signs of the times point to a new era in the history of mankind. All the sciences are leading up to a better understanding of the laws of life, to a true Anthropology, and the consequent improvement of the physical, mental and moral powers of man.

There are four or five directions toward which we may turn an expectant gaze, as in days gone by the merchants watched upon the house tops for the return of the ships they had sent out to distant ports.

Preventive medicine promises to do more and more for mankind. As the germs of many specific disorders have been discovered, so the means of their destruction have been found out. If legislation and civil administration keep up with science, if knowledge is controlled by virtue and followed by temperance, the community will be freed from many of the foes which in former generations have slain their tens of thousands.

From the chemical laboratory new remedies, as well as simpler forms of old remedies, are to be constantly looked for. The synthetical processes which now receive so much attention have lately made important contributions to the pharmacopeia. It would surprise any one whose attention has not been directed to this point to know how many claimants are awaiting judgment. Scores of substances, till lately unknown, as I have heard my colleague[7] say, are awaiting the study of competent therapeutists. Nobody can foretell what will come from their new contributions to materia medica, but one who watches the processes of discovery must feel certain that secrets hid from the beginning are ere long to be revealed, and that many of the substances already discovered have properties of the most serviceable character.

No one can say what will result from the attention that has been recently given to the study of psychical phenomena by the exact methods of science,—but the outlook is hopeful. If we are as far as ever from elucidating the mysterious inter-relationship of the mind and the body, progress has certainly been made in a knowledge of the laws by which they act upon each other. The knowledge that has been acquired in respect to the functions of the brain and nervous system has already led to the treatment of many disorders and the relief of many diseases which a short time ago were beyond the reach of remedy. We are not without hope that in the physiological and psychophysical laboratories already established here, important contributions

[7] Professor Remsen.

will be made to science which will ultimately prove to be of value to medicine and to the conduct of the body in health and disease.

Medical appliances and surgical instruments are greatly to be improved. A surgeon who has just returned from Europe, after visiting in the interest of this hospital the most celebrated instrument makers, has informed me that the processes of manufacture even now are behind the devices and requirements of surgical science. The hands of the artisan have not kept up with the brains of the chirurgeon. It is not possible to buy ready made the instruments required by this hospital.

In the near future we are to look for progress in the applications of electricity and magnetism to the treatment of disease as well as to its diagnosis. Chemistry by its synthetic methods is producing new remedies, which experimental therapeutics proceeds to test, and pharmacy then appropriates. The laws of light, heat, electricity and magnetism are found in close relationship to the problems of relief and cure. The laws of temperature and climate have their services to render. Even the influence of barometrical pressure upon surgical operations begins to be noticed. The study of the nervous system is sure at no distant day, to make important contributions to the welfare of man. Psychology is waiting for the results. Experimental physiology is doing its part. Pathology, a term as old as Hippocrates, has become a new science within the last few years. The laws of descent have but just begun to assume a scientific form. Preventive medicine is almost a new conception. The morality of personal hygiene is a new department of ethics. Biology, after having met with the same critical reception with which anatomy, astronomy, geology and chronology were greeted, may yet be honored as leading to the highest and noblest conceptions of humanity; anthropology, and the knowledge of man in his relations to the universe in which he is placed, may sum up finite knowledge.

So all along the line, in the laboratories of the university and in the wards of the hospital, knowledge is contributing to the welfare of man. The days of the coming man may not always reach the full allotment to which Chevreul has just attained, but perhaps to die at seventy will be to die in youth, and to reach the age of eighty or ninety in health and vigor, will be the rule and not the exception. Nor is length of

days our only hope. The disappearance of epidemics, fewer days of confinement in sickness, fewer "minor ailments," a decrease of infantile mortality, greater powers of resistance to the evils of certain occupations, and comparative immunity from many infirmities which are now common, artificial reinforcements and replacements of bodily defects, simpler and surer means of diagnosis, the detection of the nature, origin and history of specific affections,—and finally the assurance of euthanasia. These, as it seems to a layman, are reasonable expectations which the nineteenth century holds out to the twentieth. Can any outlay be too great if humanity is thus benefited?

To the attainment of these noble aims, "the relief of suffering and the advancement of knowledge," the foundations of Johns Hopkins are forever set apart. On the one hand stands the university, where education in the liberal arts and sciences is provided, and where research is liberally encouraged; on the other hand stands the hospital where all that art and science can contribute to the relief of sickness and pain is bountifully provided. Is there anything wanting? Yes, —there is still a great want to be supplied, an arch to rest upon these pillars. An institute of Medicine and Surgery, a College of Physicians and Surgeons, a Medical School,—the office of which shall be to promote the training of young physicians, and the encouragement of medical science is imperatively needed. Is it too much to say that there is not such an opportunity on the face of the globe, for another Peabody or another Hopkins to benefit his fellow men?

The university needs all it has, and more, to carry on the non-professional courses to which its funds are appropriated. The hospital, with all its readiness to co-operate in the advancement of knowledge will, after all, remain as I have said before, and cannot say with too much emphasis,—the home of the sick, the feeble, the injured and the dying. It is the house of mercy, not the hall of philosophy. But in close alliance with both these foundations there is a place for a school of medicine, which may bear its founder's name, and may render services as significant and memorable as those of Salerno and Bologna, at the beginning of the modern era; as those of Leyden and Edinburgh where the earliest American physicians received their education; or as those of Berlin and Vienna to which so many students of this decade resort.

This grateful city should no longer delay placing upon one of the squares near the monument of Washington, the figure of Johns Hopkins, with such designs as an artist, and an artist only, could devise, to typify the great ideas which underlie his gifts,—"the advancement of knowledge and the relief of suffering." Then might some friend of this hospital place beneath this dome a copy of Thorwaldsen's Christus Consolator, with the outstretched hands of mercy, to remind each passer-by—the physician and the nurse as they pursue their ministry of relief; the student as he begins his daily task; and the sufferer from injury or disease, that over all this institution rests the perpetual benediction of Christian charity, the constant spirit of "good will to man." Upon one hill of Baltimore rises a temple, "whose guardian crest, the silent cross" is an emblem of the Christian faith; upon another, a lofty column reminds us of the patriots' hope; upon a third, the Hotel-Dieu is placed,—the house of charity. Significant triad! "Here abideth Faith, Hope and Charity, but the greatest of these is Charity."

CELEBRATION OF THE FIFTIETH ANNIVERSARY OF THE JOHNS HOPKINS HOSPITAL, 1939

On May 4, 5 and 6, the hospital celebrated its Fiftieth Anniversary. The program of the celebration conformed to the general plan announced in the April number of the Bulletin. The following is an account of certain details of the program which could not be included in the preliminary announcement.

At scientific sessions each morning, papers were read by former members of the hospital staff.

Thursday, May 4

Dr. Grover F. Powers: Developments in Pediatrics in the Past Quarter Century.
Dr. James L. Gamble: Water and Salt.
Dr. A. L. Bloomfield: Some Clinical Problems of Gastric Secretion.
Dr. A. H. Morse: A Field of Experimental Investigation intimately Allied to Obstetrics and Gynecology.

Friday, May 5

Dr. Mont R. Reid: Some Remarks concerning the Methods of Reducing the Mortality of Acute Appendicitis.
Dr. Roy D. McClure: Diagnosis and Management of Cholecystitis.
Dr. Karl Martzloff: Some Fundamental Considerations concerning Carcinoma of the Cervix Uteri.
Dr. C. F. Burnam: Radiotherapy, its Past and Future, in Gynecology and Obstetrics.
Dr. Simon Flexner: The Nuffield Benefaction and the Full-time Clinics at Oxford.

Saturday, May 6

Dr. Thomas M. Rivers: Lymphocytic Choriomengitis and its Diagnosis by Laboratory Methods.
Dr. George Whipple: Radioactive Iron.
Dr. A. R. Dochez: Current Bronchopneumonias of Unusual Character.
Dr. F. G. Ebaugh: General Consideration of the Psychoneuroses.
Dr. C. Macfie Campbell: The Court, the Clinical and the Community.
Dr. E. D. Plass: Some Observations on the Preservation of Human Blood.

On Friday, May 5, the following presentations were made:

Presentation to The Johns Hopkins Hospital of plaque in memory of Dr. Frank R. Smith by Dr. Thomas S. Cullen

Presentation to The Johns Hopkins Hospital of portrait of Dr. Thomas B. Futcher by Dr. Warfield T. Longcope

Presentation to The Johns Hopkins Hospital of portrait of Dr. Thomas R. Boggs by Dr. Arthur Shipley

GENERAL MEETING COMMEMORATING THE FIFTIETH ANNIVERSARY OF THE JOHNS HOPKINS HOSPITAL

The General Meeting commemorating the Fiftieth Anniversary was held at 3:00 P.M. Thursday, May 4, in a large tent which had been erected for the purpose on the hospital campus. The Director of the Hospital, Dr. Winford H. Smith, presided. After an Invocation by the Rev. Harris E. Kirk, the meeting proceeded as follows:

Dr. Smith: Judge Harlan, as he is familiarly known, needs no introduction to this audience, but I can not let this opportunity pass without calling your attention to certain facts in connection with his official association with The Johns Hopkins Hospital.

Henry D. Harlan became a member of the Board of Trustees in 1895, six years after the Hospital was opened. In 1903 he was elected President of the Board of Trustees, which office he has held continuously since that time. It is not uncommon for able and busy men to give their time and their talents to worthy civic and private enterprises, the purpose of which is to benefit those members of society who are unfortunate or who are ill and distressed. It is, however, rare to find a man who has served forty-four years as a trustee of a great hospital, and for thirty-six years as the President of its Board.

It has been my privilege to work with Judge Harlan for nearly twenty-eight years and I know well the amount of time and thought which he has given to the welfare of this Hospital, given unselfishly, willingly, loyally and thoughtfully, never sparing himself whenever he felt that his time and his talents were needed for the good of the Hospital. Those who have benefited by the services of this institution, whether as patients, doctors and nurses in training or as citizens in the City and State which this institution has so extensively served, owe him a debt of gratitude beyond expression.

Hon. Henry D. Harlan, President, Board of Trustees, The Johns Hopkins Hospital: We are celebrating the 50th Anniversary of the opening of The Johns Hopkins Hospital, and it is my pleasant privilege on behalf of the Board of Trustees to welcome to these exercises the great audience here assembled containing as it does, members of the City Council, members of the State and Federal Judiciary, the President and Trustees of the University, and many prominent men and women from this City and State, from other cities and states, and from abroad. We are particularly gratified at the presence of those we think of as "our own,"—surgeons, physicians and nurses who at one time or another have been connected with this Hospital, the Medical School, or its Nursing School, and having gone out to win honor and renown, have returned, some from far distant places, in

proof of a loyalty which is a source of deep satisfaction. I should like to mention names, but time forbids.

Fifty years ago, on the 7th of May, 1889, a like company of distinguished people were convened under the dome of the rotunda of the Administration Building where Thorwaldsen's statue of "Christus Consolator" now stands, in order to mark the completion of the buildings which had been in course of construction during a period of 12 years, and were then finished, equipped and ready for the reception of patients. An intimate account of the opening of the Hospital is contained in a letter which was written by Mrs. Daniel C. Gilman to her daughters who were then in Italy. I shall quote from this letter which was dated, Baltimore, May 10, 1889:

"Of course the great event of the week has been the opening of the hospital. The day was superb and all the buildings in apple pie order; grounds ditto. The exercises were in the administration building and a band of 25 instruments were in the third gallery. There was plenty of bunting and flowering plants and ladies in their gay dresses and it was a very pretty scene. Mr. Francis King made an excellent little address and Dr. Billings a very sensible one and Papa touched the popular heart as usual. I think all the speeches struck a very high note. There was no self glorification, no mere spread eagle and empty oratory but a tone of earnest responsibility in the presence of a great trust. I think every one must have been struck with it."

To accord with the direction of Johns Hopkins in a letter of instructions to the Trustees whom he had personally chosen in his lifetime, the Hospital which he had in view was to be upon a plan "which should in construction and arrangement compare favorably with any other institution of like character in this country or in Europe." It was also to be a Hospital which should be a part of a Medical School of the University for which he had made provision in his Will, and should have a Training School for female nurses. It was to receive as patients without charge "the indigent sick of this city and its environs, without regard to sex, age or color," and "a limited number of patients who are able to make compensation for the room and attention they may require," the money received from the latter class to enable the appropriation of a larger sum for the relief of the sufferings of the former class. Thus it was to provide for the rich and the poor.

Those who were then assembled, and many not there, had been watching and waiting for the opening of a new hospital of the character and for the purposes visioned by the great founder. Their's was a forward look. What would it do? What would it mean in the world of science? Would the founder's philanthropy be justified? Would there be a notable advance in medical science, as well as in the relief of suffering? Would physicians and surgeons and nurses be trained here who would become leaders in their several professions, and who would render great service to humanity? What advance in knowledge would be made, what discoveries in treatment of disease, or in surgical or medical practice?

Today we who are assembled can look back over fifty years of accomplishments,

of fruitful endeavor. We can see a long line of patients,—more than 361,000 who have been admitted to these wards; more than 6,724,006 visits to the Dispensary. We can see many helped, many cured, lives saved of children and adults, lost minds that have found themselves, blind that have received sight, broken bodies restored, new discoveries made or applied in the treatment of disease, 2918 doctors educated, 2209 nurses graduated. It is not the number but the quality of our doctors and nurses in which we glory.

If Johns Hopkins were here in the flesh, we believe he could say—"I am satisfied. My vision has not been in vain. The good which I intended has been and is being accomplished."

This is not the occasion to recite a history of the first fifty years of The Johns Hopkins Hospital. Such a history is being prepared by competent hands. Nor is it the time to mention all the great men who have worked here and have made this Hospital have a world-wide reputation. It is said that The Johns Hopkins Hospital is better known in many places abroad than the city in which it is located. A few early famous names can not be omitted, such as Welch, Osler, Halsted, Hurd, among the illustrious dead, and among the living, their great comrade, who to our joy is here today, Dr. Howard A. Kelly.

It may be permitted in order to illustrate the growth of the Hospital and its increased activities to compare briefly the Hospital of today with the Hospital when it was opened. It was then a Hospital of 220 beds. Today it is a Hospital of 936 beds. It had then what was believed to be a large endowment,—$3,000,000, providing an income of about $180,000, enough to allow about $500 a day for maintenance. Today it costs to operate the Hospital $5,181.34 a day. It has a productive endowment of $13,824,439.71, and needs an endowment twice as large. When the Hospital was opened, seventeen buildings had been erected on these grounds, built out of income after the most careful study in order to carry out the plan of the founder. How difficult it is to plan for the future. Few of these buildings have not been replaced to accommodate increased demands, and new activities. The Pathological Building, the Dispensary Building, the Amphitheatre on the Monument Street side have been replaced by great new buildings. One of the private wards on Broadway has been enlarged and is the *William Holland Wilmer Ophthalmological Institute*. The other private ward has become the Marburg Building for pay patients. We had then no Psychiatric Clinic, no Children's Clinic, no Urological Clinic, no Woman's Clinic. All of the public wards of that day except the octagon wards have been rebuilt, and the octagon wards have been modernized for semi-private patients of moderate means. The original Nurses Home has been enlarged and a new Nurses Home to accommodate 366 nurses has been erected on the southwest corner of Broadway and Monument Street. The Henry M. Hurd Hall has been built.

The enlarged Hospital has been made possible by such benefactors as the Marburg family, who have given to the Hospital a total of more than the original endowment; by James Buchanan Brady, who gave and partly endowed the Brady Urological Clinic; by Harriet Lane Johnston, to whose generosity we owe the Harriet Lane Home for Invalid Children; by Mr. and Mrs. Henry Phipps and the

Phipps family, who built and endowed the Phipps Psychiatric Clinic; by Mrs. Lucy Wortham James, who gave the Woman's Clinic; by George K. McGaw who gave the Henry M. Hurd Hall; by the William Holland Wilmer Foundation, formed under the initiative of Mrs. Henry Breckinridge, to make possible the Wilmer Ophthalmological Institute, by Helen Skipworth Wilmer, now Mrs. Athey, to whom we owe the addition to the Old Nurses Home. To these and many other benefactors, great and sincere gratitude is due.

As we contemplete the generosity of these and many friends, the loyalty of our staff, of the Director and his Associates, of our officers and our employees, the help of the Women's Auxiliary Board, and survey the accomplishments of the years that have passed, we turn to the future with confidence and high hope. We are bold enough to believe that here charity will continue to be extended, the sick and suffering relieved, doctors and nurses always better and better educated, and that there may be discovered or perfected cures for such diseases as cancer, infantile paralysis, pneumonia and other human ills, and that the name of Johns Hopkins will become more illustrious as the years pass, and that each year continuing thousands will have occasion to be thankful that he lived and toiled not in vain, and that he devoted his great fortune to the advancement of knowledge and to the relief of suffering.

And so we welcome you all today to help us rejoice as we review the past and look forward to the future.

Dr. Smith: I shall not attempt to make appropriate introductory remarks concerning each of the five speakers who are to extend Greetings to us on this occasion. It would take too long to recite their detailed, individual records. That each of them has been elected to the Presidency of the great national association which he represents is sufficient proof of their prominence in their chosen fields and of the estimate placed upon them by their professional colleagues. It gives me great pleasure to introduce these speakers.

Dr. Irvin Abell, owing to an injury sustained in a recent accident, is unable to be here in person. Dr. Abell's Greetings will be read by our own Dr. Thomas S. Cullen who for many years has served as a Trustee of the American Medical Association.

Dr. Irvin Abell, President, American Medical Association: I deem it a great pleasure and a distinct privilege to bring to the authorities of The Johns Hopkins Hospital the congratulations and felicitations of the American Medical Association upon the completion of fifty years of brilliant, constructive achievement in its special field.

The growth of institutions for the care of the sick has paralleled the march of civilization and the marvelous development of the science and art of medicine. In the beginning they were nothing more nor less than houses or homes where creature comforts were provided for the ailing. The leadership of the Hopkins has been invaluable in developing the modern conception of a hospital, an institution providing not only adequate accommodation and comfort, but qualified administration, intricate equipment, highly trained technical personnel and

scientific technique and procedures affording assurance of competent and efficient service fully meeting the requirements and standards which knowledge, experience and humanitarianism demand as the unequivocal right of the sick at the hands of those to whom their health and well being are entrusted. Today the hospital is an indispensable part of the medical program an l has kept pace with the ever increasing range of medical knowledge. With the development of the specialties suitable hospitals for the practice of such have come into being so that the hospital field of today presents a degree of specialization corresponding to that of medicine. The origin of the word hospital is significant: it comes from the Latin, *hospes*, meaning a guest. It has the same origin as those charming words hospitable and hospitality. Not only has the Hopkins been a leader in all that pertains to scientific hospital administration and service but in the consideration of its guests it has earned the undying gratitude of the thousands who have been restored to health and happiness through its kindly and efficient ministrations.

In view of the wonderful possibilities of hospital activities a suitable motto for such institutions may be found in the words of the immortal Pasteur, who said: "I hold the unconquerable belief that the future belongs to those who accomplish most for suffering humanity." Under the impelling egis of such an incentive, hospitals have become "the repair shops of broken down human machinery" and an integral part in human economy: they are not only centers of service to the individual and the community but a huge investment for the health of the nation: they foster a spirit of research, exercise a teaching function and are powerful educational factors in the diffusion of the knowledge of preventive medicine. As educational units in our great medical structure they are obligated to learning and teaching and, to be worthy of the name, must be agents in the public service. They may not be conducted primarily for gain, must not pauperize, and all individuals connected with their activities, from the executive head to the least important employee, are but servants of the same agent in the same cause, working under the same obligations to human welfare, the prevention and relief of disease, moral, physical and mental. A broadened conception of the duties and obligations of the doctor and the hospital to their respective communities, does not permit of a multiplicity of standards based on financial or social lines or upon environmental influences: neither does it permit of a lack of standard under the mistaken idea that that which is regarded as minimal is beyond reach, financial or otherwise. It applies the great moral force of man's duty to man, which by its appeal to reason as well as to sentiment, leads hospital authorities and the doctors practicing in such institutions to utilize the modern *addenda* to medical and surgical knowledge and to correlate the work of hospital management with the work of professional service to the end that the patient is assured of proper and competent treatment insofar as it is humanly possible to assure it.

In the faithful discharge of these obligations to their fullest intent, a contribution of The Johns Hopkins Hospital that has set it apart is to be found in the field of education. Imbued with the teaching and example of its distinguished staff, residents, internes, students, nurses have gone forth, and, by their attainments,

have given ample proof of the eminent position held by their Alma Mater in American Medicine. It has been a Mecca for those of the profession who desired to see an exemplification of all that is best in scientific medicine. The fame of its clinics is known and the sincerity of its work is revered throughout the civilized world. Medicine comprises a democracy of intelligence that knows neither racial nor geographic bounds: the clinics of The Johns Hopkins Hospital have been open to the world and their leaven has been a material factor in raising the level of the whole. The names of its beneficent founder, its eminent teachers, its distinguished research workers, scientists and clinicians have become a heritage of American Medicine, the stars of many now shining in the diadem of immortality. Their present successors are committed to the traditions established by their forbears and with the background of the past they salute an even more brilliant future.

Major Julia C. Stimson, President, American Nurses' Association: Upon a happy occasion of this sort it is customary to felicitate an organization upon its enviable history, to review the outstanding accomplishments of those who have gone forth from its fold and to present good wishes for the future. No task could be pleasanter than the one imposed today upon me as the representative of the American Nurses' Association. The alumnae of the great school of nursing here at Johns Hopkins have been an important part of our national association of nurses from the day of its founding in 1897 as the Nurses Associated Alumnae of the U. S. and Canada. From that day to this, the American Nurses' Association and the National League of Nursing Education have depended on Hopkins nurses for leadership and cooperation. These organizations are proud that their records show the names of Nutting, Taylor, Lawler, Jammé, Noyes, Pfefferkorn, Melby, Baker, Creighton, Ramsay, Wiedenbach, Ellicott, Wolf and Hudson in important organization work. The National Organization for Public Health Nursing holds high the names of Lent, Fox, Dyke, Dines, Bowling, Cadel, Patterson, Brockway. International nursing groups point to the names of La Motte, Carr, Fitzgerald, Baxter, Noyes and Taylor (again), Betzold and Dunbar, and honor them and many others. The Army Nurse Corps will always cherish the records of the Hopkins nurses who served so brilliantly in the World War. Doctors of this and other hospitals pay tribute to the intelligent, efficient cooperation they have received from a long series of Hopkins graduates in clinic, operating room and ward, but it is from patients, the high and the low, the rich and the poor, that the warmest tributes come for the kindly care they have experienced from the hands of private duty and special nurses who have been taught in this great institution.

One would wish for the time to recount in detail the contributions of hundreds of Hopkins nurses to their time and their community. The records are truly inspiring and more than enough to bring fame to an institution. They make their alma mater known around the world. They give glory and prestige to it and to all nurses. Leadership and vision for their profession, efficiency and devoted service to patients—that is what their reputation rests upon.

Today is a happy day as the glory of the past fills every thought. The younger nurses are thrilled and inspired by a celebration like this. They glory in their heritage and rely upon it as they face the future. It is right that they should. A background such as theirs gives assurance, stability and strength. The old ideals, the old ways were good. Sentiment and tradition are helpful. This is, however, an age of change. New things are coming; new ideas, new ways are needed. Survival and fullest usefulness always depend upon adjustment to changing conditions. A wise man has said that "we can only preserve the essence of the past by the embodiment of it in novelty of detail."* The essence of the past of this great institution is treasure indeed. Today in its need for independence of thought, for originality and initiative, courage and vision alone will be able to embody it in novelty of detail. Upon the careful choice of professional ancestors to admire and emulate, depends our future. There were some who had the courage and imagination to leave the beaten pathways, the crowded highways.

Probably most people who drive have watched "hitch-hikers" along the highways with eyes turned backward, edging slowly on, or standing still, waiting expectantly. Like most drivers, we all have wondered if they really wouldn't get further on if they kept going straight ahead under their own steam, and if they would not stand a better chance of getting where they want to be if they plodded steadfastly along with eyes facing front and took a chance on some kindly motorist volunteering a lift. When thumbers are picked up it's all a gamble where they will be landed. There is no self-determination about their progress. Soon they get dropped by the wayside again and must look backward and wait for another lucky break.

It's easy to be a hitch-hiker on the reputation of an alma mater, easy to wait for chances, easy to take what comes by and seems to offer a temporary lift. But nursing today needs planned progress for individuals and for groups. We in the national nursing organizations today have great numerical strength and greatly increasing potentialities for influence. There is widespread confidence in the purposes of our associations and growing evidence of desire on the part of members to work together for those purposes. Since the basis of our membership is the alumnae association, it is once more appropriate to give a hail to the alumnae of this school and its soon-to-be graduates, and to remind them of the claims and responsibilities and opportunities there are for them in a planned program for the future of nursing and in its ranks of leaders. The use and understanding of facts about ourselves is a first need. Information is available at our Nursing Information Bureau at Headquarters, but it cannot create an enlightened membership without the use of its facilities by all nurses. Material is there that creates a set of professional tools without which no nurse is fully equipped.

Only the high spots in our national program can be mentioned, but they are all full of interest. National studies under the Interdepartmental Committee to

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* Alfred North Whitehead quoted by Philip Cabot: *Contemporary Conditions: A Challenge for Business Men.* Harvard Business School Alumni Bulletin, July 1937.

Coordinate Health and Welfare Activities have emphasized for nursing what researches by our own national nursing organizations had already indicated, and we are preparing ourselves to be able to take our appropriate part in nation-wide plans that will remedy the lack of essential medical nursing and hospital care for thousands of our people. The most inadequate distribution of nursing service as well as the serious inadequacies in the undergraduate, as well as in the graduate, preparation of nurses for all the major fields of nursing service is alone a challenge to every thinking nurse.

Placement and Vocational Counseling do not sound like very appealing interests to us until we study the results of the reports coming in from registries all over the country, as they are printed monthly in our Journal, and read of the increasing kinds of calls for nurses that are reported and the reasons why many calls cannot be filled. Inadequate preparation is usually the reason. In that project Placement and Vocational Counseling are another challenge—and an argument against hitch-hiking.

Renewed emphasis on standards of preparation; efforts to effect a wider distribution of nurses; the coordination of nursing interests in communities; better nursing conditions in hospitals that better nursing care may be given to patients; studies of incomes and hours, of illness of students and graduates; more and better post-graduate courses; the adoption of standards for private duty nursing—all these, with the need of more and more facts about the real content of nursing procedures, facts about our schools, our registries, our boards of nurse examiners, our nurse practice acts, the ways to meet our personal needs for future economic security, the best ways to deal with the uninformed agitators in our midst or the growing numbers of what, for lack of a better name, we call the subsidiary worker—all these demand our attention and they all have a claim upon every nurse who is a truly professional person and recognizes her responsibility for those who are coming after her. No nurses anywhere owe a greater debt to their heritage than Hopkins nurses. None have had greater leaders. None have greater opportunities nor, in consequence, greater responsibilities.

Hitch-hiking in nursing may offer immediate pleasant returns, but to be worthy of the record of Hopkins leadership, informed, forward-looking planning and individual dynamic self-motivation are needed. The ANA greets you with renewed enthusiasm and invites you to take an even larger part in its activities.

Dr. Fred G. Carter, President-Elect, American Hospital Association: I am proud to be here on this occasion as the official representative of the American Hospital Association and its component members. I bring you the greetings and good wishes of the hospitals of North America, their expressions of high regard and their assurances of continued appreciation of the great work that is being done here.

In the fifty years that have elapsed since 1889 probably more progress has been made in the practical application of knowledge to health problems than had been made in the five thousand years which preceded that date. This institution has

stood out as one of the leaders in the thinking which achieved that result. The names of its men and women which have flashed brilliantly across the medical horizon in that half century, the completion of which we are now celebrating, are almost countless. The Johns Hopkins Hospital has a record of achievement of which it may well feel proud and humanity finds much in that record to be thankful for.

When we think of this great institution as a hospital we do not have in mind brick and stone and steel and mortar; we think, rather, of all of those activities and things which go to make up the service which it renders. Above everything we think of the spirit back of it all, the spirit which stimulates the use of the imagination, the spirit which promotes inquiry, the spirit which breeds healthy skepticism, the spirit which demands constant improvement. These are some of the things which the word, *hospital*, connotes. These are the qualities in which this institution finds its motivating forces.

Neither this hospital nor any other hospital is sufficient unto itself, nor have the hospitals of the United States developed as a group independent and apart from the rest of the hospitals of the world. We have borrowed and imitated, and we like to think that we have also contributed, to the end that sick people everywhere may have the benefit of collective thinking in all languages about the problems of health and disease. Throughout the universe we have established bonds of friendship and mutual helpfulness which transcend and over-shadow the barbarism and petty bickerings of better known types of international relationship. There is a cosmopolitanism and a civilizing influence about these institutions, wherever they are, which the world might note with profit.

In the light of such thoughts we gather here today to pay fitting tribute to an institution that has carried on magnificently for fifty years. There is little that I can say that will do justice to the occasion. Rather than speak further I would conclude this word of greeting by giving voice to the hope that The Johns Hopkins Hospital may enjoy, not years, but centuries of uninterrupted, useful service to mankind.

Dr. Howard C. Naffziger, President, American College of Surgeons: My first and most agreeable duty is to turn to the Board of Trustees and to the administrative staff of The Johns Hopkins Hospital and, in the name of the American College of Surgeons, tender hearty congratulations on the fiftieth birthday of this institution.

This half-century is a short period on the calendar but a most impressive one in medicine if estimated by its accomplishment and the advances in knowledge.

It is a great privilege for your guests to be able to join with you at this time. It has been a greater one for those whose good fortune has permitted them to participate in the benefits which have flowed from this source.

As individuals, we are largely concerned with our own narrow interests and our own immediate sensory perceptions. On certain occasions, however, one may feel a justifiable pride in being a member of the human race—and this is one of them. Though criticism of the concentration and misuses of wealth in individual

hands is one of the features of our times, a glance backward indicates that this period has been blessed with certain persons—far-seeing, kindly-hearted, generous souls—who have seen to it that their wealth was used in the service of their fellow beings. Such was the founder of this Hospital, Medical School and University. Future appraisal will find this period of our life-time notable for the advances in preventive medicine and the tremendously expanding bulk of scientific knowledge applied to the treatment and cure of disease, the alleviation of suffering, the restoration of health, and the nursing of the sick. These opportunities were recognized and made possible by forward-looking benefactors. Nowhere has the trust implied in such a bequest been more wisely administered than in this institution and nowhere have the rewards been greater. Seldom has a cherished wish been so well fulfilled. It is a fortunate circumstance that The Johns Hopkins Hospital has been the recipient of such liberal private benefactions for, unlike individuals whose initiative may be removed by such help, this institution has gone forward to greater accomplishment. The wisdom of the directors of your policies has received wide recognition. Your patients, your students, your nurses, the profession at large, and medical science have benefited greatly, and, with and through them, the entire world.

One cannot consider this hospital apart from the individuals who have left their imprint upon it. They have imbued it with ideals and established tradition. Transmitted to their followers is a desire to retain its kinetic energy rather than perpetuate a static movement. It seems unavailing to avoid reference to the constellations which have revolved in this orbit, centering in your institution. To enumerate the splendid contributions of the present staff is impossible, but the profession takes pride in them. To do justice to that great galaxy that still sheds its light and whose influence is still dominant would require a more capable historian; but speaking to you today as a representative of an organization of surgeons on this continent, it is my desire to acknowledge, however inadequately, a particular debt which, as time goes on, seems to become greater as our realization of it becomes keener. It is seventeen years since "The Professor" left us. Not a long time—but long enough to have seen his professional offspring to the third generation profoundly influenced by his example and teaching. His spirit lives. The extent of his influence still spreads. The accomplishments of those so heavily indebted to him for their training, guidance and inspiration, when seen in true perspective, make the figure of "The Professor," Dr. William Stewart Halsted, the dominant one in American Surgery. The living force that emanated from him seems not to lessen with the passage of time, but to strengthen. The shy, unassuming man whose personal fastidiousness was so fully expressed in his technique, is still a guiding figure.

In a period when the operative performances of surgeons were frequently characterized by their number rather than by their quality, he remained the artist to whom nothing less than surgical perfection could be the goal. The technique of this master surgeon may be seen reflected in his descendants—in their preparations for operation, in their detailed hemostasis, in their gentleness in handling

tissues, and in the use of his favored materials. Their technique is his. Would that his penetrating qualities of mind, his gift of critical appraisal and his insight could have been passed on in the same way. What one of his pupils has not been stimulated by "The Professor's" casual inquiries as to the cause for some manifestation which had come to be accepted as a matter of fact and then, with thoroughness instilled by his example, gone on to make contributions to his profession—often notable ones. Unknowingly their futures were determined by contact with him. In circles that are still widening, the Halsted tradition spreads. To your institution, surgeons have a special bond. We acknowledge with gratitude the influence and the benefits which have radiated from it.

The Johns Hopkins Hospital is young and vigorous on its fiftieth birthday. The degenerative diseases that affect the aged, have no place here. Most of the deficiency diseases can be anticipated and avoided, and neoplasms can be eradicated if recognized promptly. If the same wise foresight that has characterized your guidance in the past is maintained in the years to come, we feel not only safe in wishing you well for the future, but confident that all our desires for this great institution will be attained.

Dr. O. H. Perry Pepper, President, American College of Physicians: The American College of Physicians is deeply appreciative of the opportunity to join in this well-justified celebration of the Fiftieth Anniversary of the opening of The Johns Hopkins Hospital.

Its founder, Johns Hopkins, was a member of the Society of Friends and, in their phraseology, believed that he would "be given to see" how to dispose of his wealth. Would that today he might be "given to see" the wonderful results of his wise bequests! For the foundation of The Johns Hopkins Hospital initiated one of those major advances by which medicine progresses; sometimes it is a discovery such as those of Pasteur or Koch, sometimes a new method, sometimes a new vision stimulating others to convert the vision into reality.

From the opening of the new Hospital untrammeled by tradition, there came new life into medicine as a whole and especially into the teaching and science of medicine, for this was the beginning of real clinical teaching in this country and of the merging of student, interne, resident and staff into one coordinated team for the study of patient and disease.

Let others recall for us the whole brilliant roster of the staff and administration from 1889 to the present. As internists, the Fellows of the American College of Physicians derive their special inspiration not only from this hospital's great first Physician-in-Chief—William Osler, but also from his eminent successors—Barker, Janeway, Thayer and Longcope. Five names to conjure with; five individuals but one unbroken stream of influence; a constant spring from which there have flowed scientific advances and an endless group of internists trained in the Hopkins tradition.

Internal medicine owes much to these five Physicians-in-Chief. The field of

internal medicine would not be what it is today if Osler's Textbook and Osler's System of Modern Medicine had not been written; if Barker had not clarified the technique of modern diagnosis in his system, *Monographic Medicine*. Janeway set us a new standard in giving up the rewards of an almost limitless practice to initiate the full-time experiment; Thayer the many-sided, a leader in medicine, in medical science, in the army and in all medical societies and associations; and Longcope who has carried on the tradition: a teacher, clinician, investigator and author.

And internal medicine has learned much from the scientific studies made on the medical wards of this hospital. From here came the classical papers on the visceral manifestations of the erythema group and on polycythemia; the description of the eosinophilia of trichiniasis; the famous monograph on bacterial endocarditis and the more recent studies on the streptococcus and on nephritis, to name only a few.

President Gilman is often credited with having had uncanny skill in selecting that famous first faculty, but it seems that later choices have been just as happy. The American College of Physicians would have been proud to have counted all of these men among its members but it was not founded in time. It has, however, included in its Fellowship not only Doctor Thayer, Doctor Barker and your present Physician-in-Chief, but many of the graduates of this Hospital.

That so many different aspects of Medicine are represented here today is significant of the solidarity of Medicine as a whole and of the interdependence of its various divisions. The hospital, the doctor, the nurse, and all those agencies directed to scientific progress and medical education, graduate and undergraduate, together form that whole we call Medicine.

And it is to Medicine in this all inclusive sense that we have each devoted our lives. Some are enlisted in one branch of the service, some in another; some are grouped for one purpose, others for another; but all have joined for the duration of an endless war, striving to reach an unattainable goal. Individually and collectively, we love and serve that discipline, system, craft or art called Medicine. To advance Medicine we must give ourselves unselfishly, and we must integrate our organized efforts to this end.

Today we are celebrating not the mere existence of The Johns Hopkins Hospital for the period of fifty years, but the remarkable influence of this institution on Medicine during the past half century. This has been an era of amazing medical progress and to this The Johns Hopkins Hospital has greatly contributed and is contributing today.

It is very proper, therefore, that both as individuals and as representatives of groups dedicated to this same end, we should congratulate The Johns Hopkins Hospital upon its past achievement, its present vitality and its promise for an even brighter future. In the name of the American College of Physicians it is my privilege to deliver this greeting to The Johns Hopkins Hospital on its fiftieth anniversary.

Dr. Smith: You have taken the time from your busy lives to come here, some of you from remote cities, to help make this Anniversary meeting a memorable occasion and to extend to us your Greetings. On behalf of the Trustees, Staff and Officers of The Johns Hopkins Hospital, I thank you sincerely.

At this point I wish to take the opportunity of making a few remarks concerning the past of the Hospital and the problems of its future.

When the Committee first discussed the program for these exercises it was felt that some one connected with the Hospital should make an address dealing with the history of the hospital and its achievements. It was finally decided that you would be far more interested in hearing what others might say about the increase in medical knowledge and the developments in the art and practice of Medicine during the period under consideration and the part which this Hospital has played in such developments.

The Committee also decided that the history of events leading up to the opening of the hospital and the record of its growth and of its achievements could better be presented in printed form, which would also serve as a permanent record. In carrying out this idea the booklet which has been presented to you this afternoon was prepared for the purpose of presenting accurately, briefly and objectively the history and record of The Johns Hopkins Hospital from its early beginnings and for the first fifty years of its actual operation. We earnestly hope you will find it interesting and instructive.

Judge Harlan has said enough to indicate the growth of the Hospital in size and usefulness, and the historical booklet will furnish more detailed information.

I wish to impress upon you, however, that it is not bricks and mortar, marble and tile, or elaborate equipment which makes a hospital. Necessary as those factors are, they are merely the means to an end and in the final analysis it is the men and women who carry on the work, particularly the professional work, which makes a hospital productive and reliable.

As everyone knows, The Johns Hopkins Hospital started on its active career under the leadership and direction of a most remarkable group of men and women. Beginning with the advice and assistance of President Gilman and Dr. Billings and under the active leadership of Drs. Welch, Osler, Halsted, Kelly, Hurd, Miss Isabel Hampton and Miss Rachel Bonner, high standards were set at the very beginning and so firmly established that they have endured throughout the years.

The instruction given by Mr. Hopkins to the Trustees, that the Hospital should "ultimately form a part of the Medical School," was particularly fortunate for many reasons, but on this occasion I wish to emphasize that the connection of the Hospital with the Medical School was undoubtedly responsible in large measure for whatever success beyond the ordinary has been achieved by it. It is my conviction that without that close association the Hospital might well have been just another hospital; but because of its relationship with the Medical School, the Hospital has been able to attract and hold men and women of outstanding ability and it is they who have been responsible for its success.

Since that early group, a long list of distinguished names has been enrolled on

the Hospital roster. These men and women contributed their full share to the reputation of the Hospital while here, and many are still here, while those who went elsewhere continued to reflect credit upon this institution which played a large part in their development. The list is too long to mention them all by name and to single out some and exclude others would be unjust.

It is fitting, however, that I should mention some of those distinguished figures who have passed on, and thus pay tribute to their memory. Among these should be mentioned Jesse W. Lazear, William S. Thayer, Theodore C. Janeway, Jr., Henry M. Thomas, Sr., Charles P. Emerson, Thomas McCrae, Thomas B. Futcher, Campbell P. Howard, Frank R. Smith, Sr., Thomas R. Boggs, Joseph C. Bloodgood, William F. M. Sowers, John W. Churchman, William H. Wilmer, J. Whitridge Williams, Clemens von Pirquet, John Howland, William McK. Marriott, William W. Russell, John T. Geraghty, William S. Baer, Frederick H. Baetjer, Herbert M. Little, Otto G. Ramsey, Benjamin R. Schenck, Ernest K. Cullen, George W. Dobbin, John Hewetson, Rupert Norton, and John Clark. There were others who gave great promise and who, had they lived, would doubtless have attained distinction in their special fields.

Important as distinguished men and women are in the hospital organization, yet they could not carry on the great humanitarian work of such a large institution without the assistance of a large number of co-workers, doctors, nurses, social workers, dietitians, anesthetists, physiotherapists, occupational therapists, secretaries, clerks, mechanics and other employees. They all serve, and for the most part, loyally and efficiently. I wish to speak particularly of one group, namely, those physicians, surgeons and specialists who, year after year, serve in the Out-Patient Department, without pay, giving their services for the benefit of the sick poor. The only reward which they receive is that of gaining experience and knowledge from association with older men, and many of them continue long after they themselves have become established, and the further reward which is given to a limited number by way of appointment to the Visiting Staff which gives them the privilege of treating their private patients in this Hospital. Without this group, which at this time numbers 309, it would be impossible to operate the large Out-Patient Department in which are examined and treated as many as 1200 to 1400 patients on a single day. I wish to pay tribute to these members of the Staff, both past and present, for a great humanitarian service, little known and therefore little appreciated by the public.

Now what of the future? Who can tell what the future will bring in this changing world? A few years ago we could look forward with confidence. I think we should still have confidence; but we must recognize that the great economic and social changes which have occurred in this country and throughout the entire world, will undoubtedly affect this institution and all others of similar purpose.

The Johns Hopkins Hospital is well endowed as Judge Harlan has pointed out, yet the income from that endowment is not sufficient to enable the Hospital to meet the increasing demands of medical science and of the public.

That today we have a plant which is modern, is due to large gifts by private individuals and to the large grants which have been made either to the University or jointly to the Hospital and University, by such Foundations as the General Education Board, the Rockefeller Foundation, and the Carnegie Corporation. These foundations gave large sums for the rebuilding of the older sections of the Hospital, and for the expansion of its facilities, solely because of their interest in medical education. They were not concerned with hospital service to the public.

Can we look forward to similar benefactions in the future? It is to be hoped for, but we must not lose sight of the fact that grave economic changes have taken place and are still in process. At the same time we must realize that legislation is proposed which, if passed, will revolutionize the practice of medicine and may revolutionize the entire system of hospitalization. It has been in the making for several years and undoubtedly in the near future some such legislation will be enacted placing upon the Federal and State governments increasing responsibility, with greater participation in all methods of caring for the sick, particularly those in the lower income brackets.

If it is true, as some say, that the day of great individual fortunes is passing, and with that is passing the day of great philanthropies and benefactions, then it will naturally follow that both hospitals and educational institutions must look more and more to the State for support with which to meet that part of their costs which endowment and operating income will not and cannot cover.

The full implications of these changes cannot be realized at this time. How they will effect the professional independence of physicians, the interrelationships of physician and patient, what effect they will have on medical education, medical research and hospital development, can only be conjectured. Regarding hospitals, particularly teaching hospitals such as this, independence and freedom of development have been and are the strongest factors in the success of such institutions. To what extent will they be hampered if forced to depend more and more upon the state? This is a question of great moment and is the main reason for the doubts which arise as to the future. I ask you to keep this clearly in mind because whatever happens, you and the public generally will be affected, possibly for your good or possibly to your ill.

I mention these matters on this occasion because the future of this and similar institutions is at stake. We would indeed be short-sighted to view only our past without giving intelligent thought and study to the future.

In a communication entitled "Looking Back" which Dr. Osler sent from Oxford to be read on the occasion of the 25th Anniversary, he said:

"And binding us all together there came as a sweet influence the spirit of the place; whence we knew not but teacher and taught alike felt the presence and subtle domination. Comradeship, sympathy one with another, devotion to work were its fruits and its guidance drove from each heart hatred and malice and all uncharitableness." That 'spirit of the place' referred to by Dr. Osler has through-

out the years been one of the hospital's most valuable assets, intangible to be sure, but very real, nevertheless. Its effect upon the life of the hospital and in moulding the character of the individuals brought under its influence makes it something priceless. It should be constantly cherished and never allowed to die.

We are very fortunate in having with us this afternoon a distinguished physician who will make the address. Throughout the period in which this hospital has been in operation he has been actively engaged in teaching and in the practice of his profession.

In addition to the other titles which he holds, his colleagues have also given him the unofficial title of "Dean of American Physicians."

It is my great pleasure to introduce Dr. James B. Herrick, Emeritus Professor of Medicine, Rush Medical College and Attending Physician, Presbyterian Hospital, Chicago.

(Dr. Herrick's address appears on pp. 56–68.)

Dr. Smith: Dr. Herrick, you have done us a great honor and have placed us in your debt. Your remarks as to the record of The Johns Hopkins Hospital and the part which it has played in the development of Medicine and Medical Education during the past fifty years have been "music to our ears." We are proud that you have so evaluated the rôle of this hospital. On behalf of the Trustees, the Staff, and the entire Hospital family, I thank you sincerely for your splendid address which has contributed so much to the success of this notable occasion.

THE JOHNS HOPKINS HOSPITAL; ITS PAST AND ITS FUTURE[1]

JAMES BRYAN HERRICK, M.D., LL.D., SC.D.

Emeritus Professor of Medicine, Rush Medical College, Chicago

Fifty years ago The Johns Hopkins Hospital was opened. By its generous and wise benefactor it was dedicated to the best possible care of the sick and to the increase of knowledge. Have these purposes been fulfilled? The answer to this question might well be the text of the address that I have been invited to give today—and the honor of the invitation is deeply appreciated.

But surely it is not necessary to prove to this audience of alumni and friends that the Hospital has honorably and faithfully served the sick; that it has richly added to and disseminated knowledge. As the wag says, you admit all this.

In confirmation of this statement I refer you to reports of the Johns Hopkins Half Century Committee in which you may find a list of outstanding staff members; of alumni who became distinguished as practitioners, teachers and investigators; of contributions in the way of medical literature and noteworthy discoveries. Yes, this Hospital was set on a hill and could not be hid. Nor did it put its lighted candle under a bushel. It could be pardoned if it pointed with pride to its sons and their work and said as did the Roman matron: "These are my jewels." If success is the attaining of one's objectives, it may truthfully be said that The Johns Hopkins Hospital has been conspicuously successful. Without reciting the many well known achievements, I shall confine my remarks about the Hospital to a discussion of the reasons for its success, its significance and its future.

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A hospital, like an individual, depends for its success upon a good inheritance, a favorable environment and good luck; upon the quality

[1] An Address delivered in Baltimore, May 4, 1939, at the celebration of the Fiftieth Anniversary of the Opening of The Johns Hopkins Hospital.

of its personnel and upon the opportunities and inducements it offers for well directed work.

This Hospital inherited the characteristics and ideals of a donor whose vision was broad, whose generosity was motivated not by the desire of self-glorification but of service to others. The Trustees appreciated the sacredness of their trust. There were many expert advisers, especially John S. Billings, who realized that the buildings, no matter how modern or how suitable for the care of the sick, would be but a mere shelter from cold and rain unless they were planned for the study, the teaching and the practice of scientific medicine. And it was the greatest gift of Fortune that at the launching of this Hospital the guiding spirit was Daniel C. Gilman. He, like Odysseus, was much travelled, rich in experience and wisdom. While like Odysseus he was resourceful, he was not like Odysseus, wily. In 1872 when he was at the University of California he said it was incumbent upon that institution "to gather up the best of past experiences of every nation, the accumulations of all men before us, to bring them to bear on our society." This he did later for The Johns Hopkins Hospital and it was a part of its rich heritage. Into this Hospital was incorporated the best of the traditions of Guy's and St. Bartholomew's Hospitals of London, the Hôtel-Dieu of Paris. Hippocrates, Harvey, Laennec, Morgagni, Virchow and Huxley were donors, as well as Johns Hopkins himself.

Fortune was favorable to success in other ways. The time was ripe for the event. Such a Hospital, such a University, such a Medical School were sorely needed. It was good fortune, too, that because of his almost uncanny ability to understand people, President Gilman with courage and foresight chose as the heads of the major departments of the Hospital men who were relatively young: Welch, Osler, Halsted and Kelly. That success was largely due to these four men and their associates, to their thorough training in medicine and the cognate sciences, to their character, to their eagerness to work, to their ability to stimulate and guide others to work—all this is common knowledge.

Surely, then, this Hospital achieved success because of its heritage, its good fortune, the character and ability of its leaders and their willingness to work. What might have happened had Johns Hopkins,

seeking self-glory, imposed awkward restrictions of the dead hand; or had men of smaller caliber than Gilman, Billings and Welch been early advisers and guides; or had there been among the four men some who were of inferior mentality, idlers, men of low ideals or weak character—all this makes one reflect and feel grateful that conditions were so auspicious.

* * * *

When the significance of the opening of The Johns Hopkins Hospital, the medical school and the university is mentioned—and it is impossible sharply to separate the work of one of these organizations from that of the other—it is sometimes stated that the medical group initiated or even really discovered many things in medical education and practice that, now accepted as truisms, were then unknown. Strictly speaking, this is not an accurate interpretation of the true meaning of the event we are today celebrating. Others had declared that the task of training medical students in the humanities was unfairly put upon the medical schools; this duty belonged to the College of Arts and Science. At several schools before 1889 the medical course had been graded, lengthened and intimately integrated with the work of the arts department. Harvard had in the early 70's attempted postgraduate work in medicine. Ward work had been stressed long before, as by Boerhaave in Leyden, by Laennec in Paris, by Stokes and Graves in Dublin and by the Medical School at Tulane University in New Orleans. The use by the clinic of the laboratory and of instruments of precision, *e.g.*, the microscope, had been put into operation in Berlin by Schoenlein about 1840. One need mention only such names as John Hunter, Claude Bernard, Virchow, Cohnheim, Pasteur to show that the value of research and of experimental medicine was realized in Europe. But in this country—and to an extent in other lands as well—these laudable efforts were spasmodic or casual. No conscious attempt had been made to incorporate them in a comprehensive plan that aimed toward reaching a clearly visioned goal. The significant fact about The Johns Hopkins Hospital was that from the beginning it knew it had a high-purposed mission to fulfill. Johns Hopkins, the founder, had this vision. His Trustees were conscious of the importance of their task. Their president,

Francis King, said at the opening of the Hospital in 1889 that the event was "one not only of local but of national and even of international importance." John S. Billings was aware of it. President Gilman said, "Is not this an opportunity without parallel in the history of our country?" What this Hospital did, then, and this is its significance, was to realize its opportunity, to engage in its undertaking with a zeal akin to that of the medieval crusaders, and to achieve results that, as Dr. Osler said, surpassed their early wildest dreams.

Few in this audience are old enough fully to realize from memory alone how urgent was the need of reform in medical education in this country in 1889. The state of affairs in many medical schools and hospitals was deplorable. Proprietary schools flourished; standards of admission were low; the sessions were short; courses were often ungraded, didactic repetitional lectures were the rule; much of the work was done by teachers whose main interest was private practice; laboratories were miserably equipped or altogether lacking; libraries were the exception; anything that could be called a true university atmosphere was a rarity, as was real research. Nursing was of inferior quality. Many medical schools were without hospital facilities. As I have said, there were exceptional schools, exceptional teachers, and exceptionally good graduates, for there were giants in those days. Dr. Victor Vaughan of the University of Michigan, my own alma mater in arts, rather slyly called attention to this when in his Memoirs (1926) he stated—and as I have been informed much to the disquiet of the usually dignified, well-poised William H. Welch—that it seemed to be forgotten that "when in 1893 Johns Hopkins Medical School had opened its doors and presented its Faculty par excellence of eight full professors, four of them—Hurd, Howell, Abel and Mall—had diplomas from the University of Michigan, and two of them—Abel and Howell—had been taken directly from the Michigan Faculty." But nowhere except here in Baltimore was there a group that had the means, the vision, the definite goal, the qualified teachers and governing boards that enabled them by precept and example to set a standard whose excellence forced other schools and hospitals for very shame and in self-defense to make radical changes along the line of the Hopkins plan.

This plan revealed the advantage of having as heads of even the clinical departments salaried men whose primary interest was teaching

and service in the Hospital without the distractions incident to private practice. It proved that the sick man was better cared for in a hospital in which education was the watch word. It showed that the old saying *docendo disces* was true, for not alone was the undergraduate taught but also the heads of departments, the fellows, the residents, the interns. For there is no more potent stimulus to thorough work by an instructor than a keen-eyed student watching, asking searching questions and eagerly looking to see whether the subsequent history, perhaps the revelations of the autopsy, confirms the diagnosis or the efficacy of the treatment. Nurses were educated on a professional, not a trade, basis. The patients received lessons in personal hygiene; they saw for themselves the difference between the methods of honest scientific medicine and cults based on fantastic theories. Thus, the public was educated. The hospital showed that the activating principle that made for progress and prevented intellectual stagnation was the spirit of research in the ward and laboratory. It showed the value of the library. It was not vainglory that prompted the publishing of results, the issuing of a special bulletin and of reports. These were agents for the spread of the gospel of the New Deal in Medical Education.

It is to the lasting glory of The Johns Hopkins Hospital that it played such a leading part in bringing about the veritable revolution in medical education that occurred in this country during the last five decades. Without her example and active participation, the change would have come but only by the slower process of evolution. No impartial critic will question the statement that among the major events in American medicine of the last hundred years was the founding and operating of The Johns Hopkins Hospital.

What other significant events in American medicine are worthy of mention? Perhaps no two persons would agree as to the answer. One event of world wide importance was the discovery of anesthesia. Dr. Welch said America's greatest contribution to world medicine was made by John S. Billings who built up and developed the Surgeon General's Library with its Catalogue and Index Medicus. If events limited in their influence chiefly to this country, are considered, one should name the creation by the American Medical Association of two Councils, the one on Medical Education and Hospitals and the other on Pharmacy. The work of the one Council, in eliminating many

schools that were unfit and in raising the standards of other schools and of hospitals; and of the other Council in showing the pernicious nature of the all too prevalent practice of prescribing patent and proprietary medicines of composition unknown to the practitioner, were events of major importance that redound to the credit of the American Medical Association and its great editor and secretary, George H. Simmons. One should mention in this category of significant events the endowing by men of wealth, of institutes and foundations to aid in medical research, education and practice; also the remodeling of the American Medical Association and its phenomenal growth to a membership of more than 100,000 members, Mr. Abraham Flexner's report on medical education, the rise of specialism, the development of group clinics, the formation of local and national special societies; though there are those who would question, and perhaps with justice, whether some of these events have resulted in unmixed good.

I wish to put into the class of major events the work of William Osler and in particular the publication of his Textbook on Medicine. I am not unmindful of the services of the others of the so-called Big Four of the Johns Hopkins group—Kelly whose operative skill excited admiration and who showed the value of artistic illustration in medical writings; Halsted who, though he worked unostentatiously, stimulated others to thorough and scientific study of the pathology of disease and the improved technic of operations. Above all I would not minimize the value of William H. Welch, whose constructive ability was responsible for many of the early as well as later developments of the Hopkins Hospital, who was the balance wheel of the medical group, the philosopher of great knowledge and broad views whose wise counsels were often sought from far beyond the confines of Baltimore and the Hopkins Hospital. Without meaning to rob anyone of these three of the just credit which is his due, I wish to state my belief—perhaps as a clinician in the field of internal medicine I may be prejudiced—that the influence of William Osler on the practice and teaching of medicine was as great as, perhaps greater than, that of any other medical man in the English speaking world in the last one hundred years. Sir Humphry Rolleston has recently said that Osler at the time of his death was the greatest personality in the medical world.

It is not easy to assess at its real value the influence of a truly great

man. Nor is it possible always to discover the secret of such influence. Dr. Osler made many valuable contributions to medical knowledge, yet he is credited with no epoch-making discovery. He was an excellent diagnostician and clinician, yet some of his students and colleagues were regarded as his equals in these respects, perhaps even his superiors. Though an effective speaker he had no surpassing gift as an orator.

But the favored few—students, staff members and colleagues—who in the ward, the lounge, his home library or in the meetings of societies so many of which he started, came into intimate contact with him were, by the magic of his unique personality, stimulated to search at the bedside, in the laboratory, the morgue, the library for the truths of medicine both the old and the new. They were led, unconsciously perhaps, to appreciate the meaning of culture, scholarship and character in the physician. They saw how one whose vocation was science and medicine could yet become famous as a man of letters and a lover of books. William Osler exemplified Lord Tweedsmuir's three qualities of greatness: humility, humor, humanity. Though unusually well informed, he was humble before the huge mass of new knowledge only a portion of which could be grasped by any one man. His sense of humor made him conscious of his own and others inconsistencies and frailties and saved him from many a spell of deadening depression. He was humane, human. Essentially an aristocrat, he was yet democratic in his mode of life, tolerant and accepting all men as brothers. From him, his graduates and staff there emanated an influence for good that lifted the practice of medicine over a wide area to a higher level than was before known.

But his great contribution was his Textbook on Medicine. This has been rightly termed by Harvey Cushing "Osler's medical masterpiece." One might well defend the thesis that it was the greatest single contribution made by The Johns Hopkins Hospital or The Johns Hopkins Medical School. It was a carefully edited compendium of the essentials of medicine. Bewildering theories and unproven facts were omitted. Useless or harmful therapy was condemned. Unnecessary verbiage was deleted. In fine, it was an epitome of the truths of practical medicine reduced to lowest terms, stated in clear, direct language, yet so shot through with the individuality of the

author and his sane judgment that it impressed the reader as not a mere compilation of facts but as a carefully prepared summary that, like a lawyer's brief, presented the facts fully while at the same time, like a judge's charge, it interpreted them fairly. It went to the desk of medical students, to the library of the general practitioner and the reference shelf of the specialist. Like a breeze through an opened window of a room stifling with the drowsy burden of rebreathed air, it roused the profession to an appreciation of the truer meanings of scientific medicine. It is a wellknown fact that it had a decisive influence in inducing laymen to contribute enormous sums to further medical research and to sustain efforts in this country and elsewhere to prevent and combat disease. It was a most potent connecting link between medicine and the public.

Many years ago President William Rainey Harper said to me that though he himself was a devotée of research, and the president of a university the major activity of which was research, he was unwilling to say that the work of the one who sought for new facts was of greater value than that of the teacher or the writer of a genuinely good textbook who made known and interpreted the old. Such a useful service was rendered by the textbook of William Osler.

* * * *

Today alumni, members of the staff and friends of The Johns Hopkins Hospital have gathered in pride and loyalty to celebrate the close of fifty years of splendid service to medicine and humanity. But this occasion should be regarded not alone as the close of an era but also as the beginning of a new one. An individual, as age creeps upon him, may after a half century of honorable toil feel that he has reached his goal and that he is satisfied. But a hospital, unlike the individual, is not to pass away; it is to endure; it should never be satisfied. For it, the goal is constantly receding, never quite reached. In an institution such as a hospital, contentment with achievement connotes not health but degeneration and decay. This Hospital, if it is to progress, should today re-dedicate itself to carrying out the noble intentions of its donor and its founders. But these intentions must perforce be modified so as to fit altered conditions.

May I read to you a few sentences from the address given in 1876 by Thomas Huxley at the dedication of The Johns Hopkins Univer-

sity? In speaking of the future growth in population and importance of the United States, he said: "You and your descendants have to ascertain whether this great mass will hold together under the forms of a republic, and the despotic reality of universal suffrage; whether state rights will hold out against centralisation, without separation; whether centralisation will get the better, without actual or disguised monarchy; whether shifting corruption is better than a permanent bureaucracy; and as population thickens in your great cities, and the pressure of want is felt, the gaunt spectre of pauperism will stalk among you, and communism and socialism will claim to be heard. Truly America has a great future before her; great in toil, in care, and in responsiblity; great in true glory if she be guided in wisdom and in righteousness; great in shame if she fail." On that momentous occasion sixty-three years ago, Huxley spoke not alone with the silver tongue of the orator but with the voice of the prophet who foretold the dangers that threatened our civilization. That he had the clear vision of the seer we must admit when we note that the profound economic, political, social, philosophic changes that he predicted are with us today.

Since Huxley's time science also has been revolutionized, as witness relativity, the quantum theory, radium emanations, cosmic rays. Medicine has shared in all this. X-rays, vitamins, endocrinology, electricity as applied in diagnosis and treatment, synthetic drugs, some with almost specific reactions, the rise of biological chemistry, psychiatry, genetics, preventive medicine—merely to recite these names of subjects still in the active stage of development makes it clear that in the next fifty years the Hospital will have a stupendous task to make suitable readjustments in many fields.

Yet we may be sure that in the future which now seems so chaotic there will be found some type of hospital made up of three elements: the buildings or plant, the patient, the doctor. And there will be some form of education which, we trust, may not have lapsed into mere experience and empiricism. It would be presumptuous in me to discuss many problems that are your private concern. I trust, however, I may be permitted to call attention briefly to some that are in a sense of semipublic interest, especially some relating to educational features. I do this with a full consciousness that changing conditions

may make these suggestions seem unreasonable and foolish, and that a plan that today seems sound or even radical may tomorrow be outmoded.

You will have, you undoubtedly already have, plans for new or remodelled structures and better equipment. You are concerned with ways and means for balancing your budget. You are perhaps hoping that good friends may realize some of your urgent needs and offer financial help. May your worthy prayers be answered. It is well to recognize, however, the danger of emphasizing quantity at the expense of quality. Too great size may mean unwieldiness. Your director has estimated that accommodations for a maximum population of patients, doctors, nurses and all others engaged within the walls could well be limited to 2000, of which number 900 would be patients. Such conservatism seems wise.

For our purpose today, hospitals may be divided into three groups, though the lines separating these types are not always sharply drawn: those that only care for the sick; those that are designed mainly to teach; those the primary purpose of which is research. According to the will of its benefactor and the early purposes of its founders, The Johns Hopkins Hospital has had characteristics of all three of these types; it has rendered service to the patient, has disseminated knowledge already known and has contributed knowledge that was new. It would seem proper that it should continue to maintain this threefold character.

What is commonly called pure research may be carried on in the hospital laboratory, library or in the field. It may be done by the few who are competent, who in segregated wards with selected patients devote all their time to the study of special problems.

On the other hand the physician who in the ward cares for the patient and carries on instruction, should be accorded a rank of equal dignity. He too is activated by the spirit of research. He sees in every patient a small problem for investigation. His study of some unusual case or of groups of patients may lead him to conclusions that are of immediate practical value, or that may touch more remotely upon principles of fundamental importance in medicine. Jenner did more than discover the practical procedure of vaccination; his work had a distinct bearing upon the subject of immunity. Dr. Welch

once remarked that much of the most important knowledge in medicine had come from physicians who had labored in the wards. In the future, may there not develop from such clinical research some Jenner, Laennec, Morgagni, or Bright? And may there not be place for research by public health experts, social service workers, nurses and students of economics and of medical history?

Fifty years ago the *bête noir* of some leaders in medicine was the specialist. Medical schools and hospitals, we were told, were to train for general practice alone. There is still need for the most carefully planned training for the general practitioner. He will be of a new type; he cannot be the man who knew all and did all as in "the horse and buggy days." He will have to be unusually well informed. While caring for a large proportion of the ailments of his patients his function will often be to advise as to consultants and hospitals for special diagnosis or special treatment. Specialism is a necessity; it has come to stay, must be reckoned with and trained for. Closely related to specialism is postgraduate and graduate education that is bound to bulk large in the near future, particularly since certification for specialism is being urged. The hospital will have to recognize these as important educational problems that will demand careful study and perhaps many readjustments.

In some medical schools and hospitals there is too much standardization. There is little room for the play of individuality. The undergraduate is forced to do something in the way of investigation, though he may not be fitted for it and may not desire it. The resident, aglow with the divine ardor for research, must concern himself with the routine of class instruction; the associate or head of a department must use his time and energy largely in executive and administrative work though he may have been chosen for his outstanding ability as an investigator, a teacher or a clinical physician or surgeon. These faults should be corrected. But usually it is better to find the round peg for the round hole than to try by whittling to make the square peg round or the round hole square.

In this connection I recall a conversation I had with Dr. Thayer a short time before his death. He lamented this tendency of which I have just spoken. He cited instances of men of unusual ability who, after long periods of investigative work largely in the laboratory, had

tried in vain to come back as clinicians. The early impressionable years, the years of initiative had gone. The apprenticeship of the ward with its intimate contact with patients had been lost, the skill in diagnostic technic that is attained only after long experience at the bedside could not be easily acquired after forty. And similarly he cited the cases of men who would probably have been better investigators than they had been clinicians. I agreed fully with Dr. Thayer. I convey this thought as a message to you from one of the most skillful and best beloved of your clinicians.

In a sense the hospital staff is a group of specialists. To work effectively there must be well integrated harmonious teamwork. To exalt the function of one group over that of another—internal medicine over surgery, the laboratory over the ward, the library over the morgue, experience over theory, research over instruction—this is unfortunate even disastrous. Aesop in his fable taught how foolish it was to dispute as to which organ of the body was the most important. So it should be recognized that every department in the hospital, though autonomous in many respects, is intimately related to, and mutually dependent upon, all the others.

And now may I inconsistently declare that there is one person in the hospital that is, or at least should be, supreme? I mean the physician—I am using the term "physician" in its broader sense, not limiting it to the internist—who is in charge of and closest to the patient. He will call for help upon the laboratory, the instrument of precision or his expert colleague. Yet he is aware of the fallibility of all these aids. He recognizes the danger that the specialist, like the microscopist when he uses only the high power lens, may see but the restricted field, thus missing the proper relation of parts. No matter how strongly we advocate the specialist, the laboratory, the instrument, we must find a place of authority in our hospital for the doctor who interprets the assembled facts as they concern the one particular patient whose disease problem he is trying to solve. He alone knows the complete history, the psychic and social factors, the condition of this patient's body as a whole. He alone is to tell which of the many symptoms or findings are of significance in this particular case. He must decide as to the management. If I may state it extravagantly, he is not only both jury and judge but prosecuting and defense at-

torney as well. And he must be a man of a dual personality. He must be relentlessly, heartlessly scientific toward the disease yet humane toward the patient. In the patient he sees more than a case; he sees a human being with whom he suffers, i.e. is sympathetic.

It may be impossible to predict the type that will evolve from your present Johns Hopkins Hospital in the next fifty years, what will be the changes in buildings, in economic, social and educational features, but of one thing we may be sure: that two figures will still be with you, constituting what L. J. Henderson has called a social system. These will be the doctor and the patient. These two elements of the system should not be too far separated. The best service will be rendered when there exists something akin to the intimate relation which prevailed when the old family doctor was guide, philosopher and friend. Wholesale, routine, robot-like service will be one of the greatest dangers of the future hospital. May The Johns Hopkins Hospital escape it.

In conclusion, may I congratulate you on your glorious fifty years of service. If to-day you are not as formerly *facile princeps*, for others have been catching up with you, you are still in the front rank and are still looked to for leadership which in these parlous times is sorely needed. If you remain true to the original intent of your founders, at the close of another half century your Hospital will be, as of yore, a leader in the care of the sick, in the dissemination of helpful knowledge and in the discovery of the worth while new in scientific medicine.

THE CLINICAL AND PATHOLOGICAL FEATURES OF CARCINOMA OF THE BODY AND TAIL OF THE PANCREAS

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Most text-books of medicine, surgery and pathology convey the impression that carcinoma of the pancreas almost always arises in the head of that organ, and that carcinoma of the body or tail of the pancreas is so rare as to be scarcely worthy of consideration. It must be admitted that primary carcinoma of the body or tail of the pancreas is by no means common. Nevertheless, cases are encountered not infrequently in the larger hospitals and clinics, and such cases invariably offer a nice problem in diagnosis. In spite of surgical exploration the diagnosis may remain obscure until established at autopsy.

The clinical syndrome characteristic of carcinoma of the head of the pancreas has become more and more familiar since its recognition and description by Bard and Pic (2) in 1888, but Chauffard's description (5) in 1908 of carcinoma of the body of the pancreas as a distinct clinical entity evoked less interest. The contributions of Leriche (19) and Malus (21) in 1910 likewise received little attention and it is only within very recent years that any attempt has been made to delineate more clearly the clinical features of carcinoma of the body or tail of the pancreas. So far as I am aware, the only systematic study directed toward this end is that of Ransom (24) who analyzed a series of 16 cases in which the diagnosis was established at operation in 14 and at autopsy in 2. He found, in agreement with previous authors, that the disease was characterized most constantly by severe upper abdominal pain frequently occurring in paroxysms, rapid and extreme emaciation and complete absence of jaundice. An abdominal tumour was palpable in one half of the cases. X-ray studies suggested the diagnosis in one fourth of the cases, but laboratory tests were of little

assistance. In 11 of the 16 cases, carcinoma of the pancreas was apparently quite unsuspected prior to operation or autopsy, a fact which emphasizes the difficulties of clinical diagnosis.

In view of the paucity of the literature on the subject and the clinical difficulties presented by cases of carcinoma of the body or tail of the pancreas, it seems worth while to record an analysis of the clinical and pathological features of a series of cases in which the

TABLE I

Location of primary carcinoma of pancreas

AUTHOR*	HEAD	BODY OR TAIL OR BOTH	WHOLE PANCREAS	LOCATION UNDETERMINED OR UNRECORDED	TOTAL NUMBER OF CASES
Ancelet (1)	36	11	88	65	200
Biach (3)	19	13	31	10	73
Lanceraux (18)	11	4	0	0	15
Oser (23)	20	5	1	6	32
Heiberg (13)	23	7	5	0	35
Kiefer (17)	24	5	4	0	33
Wallau (29)	169	36	0	125	330
Hick and Mortimer (15)	22	23	4	0	49
Ransom (24)	58	16	0	0	74
Leven (20) (Hospital series)	22	2	6	0	30
Leven (20) (Autopsy series)	60	19	18	0	97
Futcher (10)	29	0	0	2	31
Rienhoff and Lewis (25)	75	6	6	22	109
Present series	28	19	3	0	50

* The names of Boldt (Statistische Uebersicht der Erkrankungen des Pankreas nach den Beobachtungen der letzten 40 Jahre. *Inaugural Dissertation. Berlin*, 1882) and Mirallié (Cancer primitif du pancréas. *Gazette des Hôpitaux. Paris* 1893, **66**: 889.) are not included in the table because the statistics commonly credited to them in the literature are not to be found in their original papers.

diagnosis was established at autopsy, especially with the object of drawing attention to the tendency of this type of cancer to spread in such a manner as to produce clinical signs and symptoms not hitherto recognized as common in this disease.

Among the first 14,000 autopsies performed in the Department of Pathology of the Johns Hopkins University, there were 50 cases of primary carcinoma of the pancreas, comprising 28 cases of carcinoma of the head of the pancreas, 7 of the body, 10 of the tail and 2 of the

body and tail. In 3 cases the whole pancreas was diffusely involved. The total number of cases, therefore, in which the carcinoma arose in the body or tail of the pancreas without involving the head was 19. This seems an extraordinarily large number in comparison with the figure of 28 for carcinoma of the head of the pancreas which is generally conceded to be much more common, but this large proportion is equalled and even exceeded in some of the series of cases reported in the literature as is shown in Table I in which are collected the statistics of a number of authors.

The great variation in the figures given by different writers is to be explained by the fact that the cases were collected in some instances from clinical records and in others from autopsy records, and it is fairly obvious that the two methods of approach would yield somewhat different results for a number of reasons. First of all, the clinical diagnosis of carcinoma of the head of the pancreas is not often overlooked, while carcinoma of the body or tail of the pancreas is seldom diagnosed during life. Moreover, carcinoma of the lower end of the common bile duct may be erroneously diagnosed as carcinoma of the head of the pancreas (27). Thus, the statistics compiled from clinical records are likely to give too high a figure for carcinoma of the head of the pancreas and a figure much too low for carcinoma of the body or tail of the pancreas. On the other hand, statistics derived from autopsy records are likely to err in the opposite direction because of the common practice of allowing patients to leave the hospital after the diagnosis of carcinoma of the head of the pancreas has been established and palliative treatment instituted. Such patients, dying at home, seldom figure in autopsy records, while in the case of patients suffering from carcinoma of the body or tail of the pancreas, the clinical diagnosis is usually problematical and extra efforts are put forth to keep the patients under observation in hospital and to obtain permission for autopsy. Such cases, therefore, appear in disproportionate numbers in autopsy records. Interesting examples of the discrepancy between clinical and autopsy statistics are afforded by the contrast between Leven's hospital series and autopsy series (20) and by comparison of the results of Futcher (10) and Rienhoff and Lewis (25), based on clinical studies in the Johns Hopkins Hospital, with my own figures drawn from the autopsy records of the same institution, all of which are included in Table I.

Altogether, it is extremely difficult to estimate the true frequency of carcinoma of the body and tail of the pancreas, but allowing for the sources of error already pointed out, one may perhaps hazard the guess that carcinoma of the body and tail of the pancreas occurs with about one third the frequency of carcinoma of the head of the pancreas.

In any event, the incidence is probably much higher than is generally believed.

The sex and age incidence of carcinoma of the pancreas in the present series corresponded with that reported by others. The 50 cases comprised 38 males and 12 females. The age distribution was as follows: second decade 1 case, third decade 3 cases, fourth decade 7 cases, fifth decade 10 cases, sixth decade 16 cases, seventh decade 10 cases, eight decade 1 case, ninth decade 2 cases. The largest number of cases, 16, occurred in the sixth decade, and the average age of all the cases was 51.2 years. The youngest patient was a coloured boy, 18 years of age, and the oldest a white woman of 83 years, both of whom had carcinoma of the body of the pancreas. The proportion in this series of 36 whites to 14 negroes does not support so strongly the suggestion of relative immunity on the part of the coloured race, as do the figures of Futcher (10) and Hick and Mortimer (15). In the group of cases of carcinoma of the body and tail of the pancreas there was no significant difference from the remainder as to sex, age or racial incidence.

It is not the intention to analyse in this paper the cases of carcinoma involving the head of the pancreas. Suffice it to say that these cases conformed in their clinical and pathological manifestations to the descriptions to be found in the literature (9, 10, 14, 15, 17, 20, 25, 28) except that, contrary to the statements of some, abdominal pain was one of the most prominent clinical symptoms, occurring at some stage of the disease with the same frequency as jaundice.

The cases to be dealt with in detail here are those in which carcinoma originated in the body or tail of the pancreas without involving the head. Of the 19 cases of this kind in the series, the first two lacked sufficient clinical and pathological data for the present analysis. One other case, brought in from outside the hospital for autopsy, must also be omitted for lack of a clinical history. The remaining 16 cases of carcinoma of the body or tail of the pancreas in which adequate information is available have furnished the material for analysis. In addition, the 16 most recent consecutive cases of carcinoma confined to the head of the pancreas have also been studied in detail and will be referred to wherever striking differences or similarities warrant comparison with the cases of cancer of the body or tail of the pancreas.

CLINICAL FEATURES

The most common initial symptoms in the 16 cases of carcinoma of the body and tail of the pancreas were, in order of frequency, abdominal pain in 14 cases, obstinate constipation in 6, belching of gas or eructations after meals in 6, swelling of the abdomen in 5 and weakness in five. Anorexia, always associated with abdominal pain, was complained of in 4 instances and loss of weight in three. The 2 patients who did not have abdominal pain among their initial symptoms first noticed weakness and loss of weight. One of these patients also had "vague indigestion" and belching after meals, but abdominal pain appeared about 6 weeks later. In the other case, there was never at any time any real pain, only slight epigastric discomfort relieved by eating. Constipation, when it was noted as one of the first symptoms, frequently preceded the appearance of pain by one or two weeks. Swelling of the abdomen proved to be due to ascites in every instance. In not a single case was jaundice among the first complaints.

All of this is in marked contrast to the onset of symptoms in the 16 cases of carcinoma of the head of the pancreas. Among these cases, jaundice was one of the initial complaints in 13 and abdominal pain in only 5 cases. The pain never began more than one week before the appearance of jaundice. Other symptoms complained of at the onset were most inconstant and no single symptom other than jaundice or abdominal pain occurred in more than 3 of the 16 cases. These miscellaneous symptoms, occurring in different patients, included nausea, vomiting, eructations and belching of gas, a feeling of fullness in the abdomen, anorexia, diarrhoea, weakness and loss of weight. The 3 patients who did not complain of jaundice at the beginning of the illness never became jaundiced at any time through the whole clinical course. In two of them the sole initial complaint was persistent vomiting. In the third case, there was weakness and pain in the back. Constipation or swelling of the abdomen did not occur as initial symptoms in any of these cases of carcinoma of the head of the pancreas.

The progressive clinical course of the patients with carcinoma of the body and tail of the pancreas was marked by symptoms among which the most constant were those emphasized by Ransom (24) and previous writers, namely loss of weight and abdominal pain. But

some of the other symptoms and signs, while not so constant, seem equally important and worthy of emphasis because they may be so misleading if one is unaware that they are common manifestations of this disease.

Loss of Weight. All of the 16 patients with carcinoma of the body or tail of the pancreas had definite loss of weight, presumably accompanied by loss of strength, during the course of their illness, and in the majority of cases the weight loss was extreme. So, too, in the 16 patients with carcinoma of the head of the pancreas, loss of weight was an outstanding feature in the great majority of cases. However, it was not determined in this study whether the loss of weight was any more or less marked in association with carcinoma of the body or tail of the pancreas than with carcinoma confined to the head of that organ.

Abdominal Pain. In 15 of the 16 cases of carcinoma of the body or tail of the pancreas, abdominal pain was a prominent symptom. It appeared in 14 cases as an initial symptom and in one other case pain began about 6 weeks after the onset of other symptoms. One patient in whom the tumour was located in the tail of the pancreas was completely free from pain throughout the illness and suffered only from slight epigastric discomfort relieved by eating. In 10 cases the pain was more or less constant and dull, aching or boring in character. In 3 of these cases, paroxysms of severe abdominal pain were superimposed. In 3 other cases, attacks of severe paroxysmal abdominal pain were separated by intervals of relative comfort. Two patients had attacks of colicky pain in addition to constant dull pain and two other patients had no constant pain but only intermittent attacks of severe colicky pain.

The pain was located most frequently in the mid-epigastrium. Constant dull pain was always felt in the epigastrium or else in the region of the umbilicus, the former in 7 cases and the latter in 3 cases. In the 6 cases in which paroxysms of pain occurred, they were felt in the epigastrium in 2 cases, in the right hypochondrium in 2 cases and over the whole abdomen in 2 cases. Colicky pains were referred either to the lower abdomen or were felt over the whole abdomen and did not radiate. Abdominal pain other than that of a colicky nature had a definite radiation in 6 cases. In every one of these cases the tumour

was located in the tail of the pancreas and the pain in every instance radiated to the left side, either to the left hypochondrium or across the lower part of the left chest. In one case the pain radiated around both sides to the back. In the great majority of cases the pain had no relation to the ingestion of food, but in 4 instances direct questioning had apparently elicited the description of a vague and inconstant relation to meals. In two cases, the pain was worse at night, when the patient was lying down.

While abdominal pain was an important symptom in almost all of these cases of carcinoma of the body or tail of the pancreas, it is evident that there is no constant type or location of pain which is common to all or even to a majority of the cases, much less any special characteristic of the pain which is peculiar to this disease alone. The same was true among Ransom's cases (24). Only one feature seems especially striking and that is the radiation of pain to the left side. This occurred in 6 cases in all of which the tumour was located in the tail of the pancreas. Radiation of pain to the left did not occur in any of Ransom's 16 cases (24) but the tumour occupied the tail of the pancreas in only 4 of them. In the series of 16 cases of carcinoma of the head of the pancreas, abdominal pain was encountered as an important symptom at some stage of the disease in 12 instances, but radiation of the pain when it occurred was always to the right side. Radiation of upper abdominal pain to the left is perhaps rare enough in other diseases which might be confused with carcinoma of the body or tail of the pancreas that this symptom may be emphasized as a point of considerable importance in differential diagnosis. Chauffard (5) emphasized as a characteristic point the onset of abdominal pain in the left hypochondrium and a shift of the pain, later in the course of the disease, to the midline or even to the right, but this phenomenon was not observed in the present series.

Constipation. Obstinate constipation was mentioned prominently as one of the first symptoms to appear by 6 of the 16 patients. In 5 other cases, constipation appeared as a troublesome symptom somewhat later in the course of the disease. Ransom (24) recorded definite constipation in 13 of his 16 cases. Constipation is known to be a common symptom also in cases of carcinoma of the head of the pancreas (17, 20, 25, 28).

Ascites. Perhaps the most striking clinical feature of this series of cases was the frequent occurrence of ascites. Swelling of the abdomen which proved subsequently to be due to ascites was among the initial complaints of 5 patients, and ascites was recognized in 5 others by physical examination, making a total of 10 of the 16 patients who suffered from ascites over a period of from 2 weeks to 4 months before death. Ascitic fluids withdrawn by paracenteses or escaping at operations were described as clear or only slightly cloudy straw-coloured fluids; in no instance was the fluid grossly sanguinous or even blood-tinged. The high incidence of ascites in this group of cases is in striking contrast to its occurrence in only one of the 16 cases of carcinoma of the head of the pancreas. The presence of fluid in the abdomen in this case was recognized clinically on the day before death and at autopsy an acute bile peritonitis was found as the cause.

Ascites has been noted by various authors as an occasional accompaniment of carcinoma of the pancreas, but the custom of considering together all cancers of the pancreas, no matter where they are located, renders it impossible to collect extensive statistics from the literature to support the obvious suggestion that ascites is common in association with carcinoma of the body and tail of the pancreas, and is rare as an accompaniment of cancer of the head of the pancreas. However, some information may be gained from the few publications in which protocols of cases are included:

Herringham (14) reported the occurrence of ascites in 6 of his 17 cases, but in all of the six, either the whole pancreas was involved or the tumour occupied the body of the pancreas as well as the head. Speed (28) found that ascites had occurred in about 20 per cent of his 52 cases. Of these cases, 11 came to autopsy and the anatomical diagnoses are included in his paper. Some of the cases were diagnosed as "carcinoma of the head of the pancreas" and jaundice was noted, but in the 4 cases which came to autopsy with ascites there was no jaundice and the anatomical diagnoses read simply "carcinoma of the pancreas," suggesting that the tumours had occupied some part of the pancreas other than the head. These 4 cases account for almost half of the total of 20 per cent of the whole series in which ascites was found. Kiefer (17) reported ascites in 3 of his 33 cases of carcinoma of the pancreas. In one of these the tumour was located in the tail of the pancreas; in the second the cancer involved the whole pancreas, and in the third the position of the tumour in the pancreas was not described in the autopsy report.

Even on the basis of the details available in these three papers alone it is perhaps permissible to suggest that the majority of the reported instances of ascites may well have occurred not in the cases of carcinoma confined to the head of the pancreas but in those in which the tumour involved the body or tail.

Hematemesis and Blood in the Stools. Vomiting of blood, blood clots or coffee-ground material, was recorded in 8 of the 16 cases of carcinoma of the body or tail of the pancreas. In 4 cases hematemesis occurred only once but in the remaining 4 cases it was repeated on two or more occasions. Blood clots in the stools or tarry stools were recorded in 3 cases, and in 3 additional cases application of the guaiac test to the stools gave a strongly positive reaction.

Among the 16 cases of carcinoma of the head of the pancreas, coffee-ground vomitus on one occasion was reported in one case, and in one other case blood was vomited on the day after a cholecystgastrostomy had been performed for the relief of jaundice. None of the other cases ever had hematemesis. In no instance did gross blood appear in the stools, nor were tarry stools recorded, although benzidine or guaiac tests on the stools were positive in 6 cases, in 4 of which cholecystgastrostomy had been performed shortly before.

Dilatation of Superficial Abdominal Veins. In 2 of the 16 cases of carcinoma of the body or tail of the pancreas dilated and distended superficial veins were observed coursing over the abdomen and lower chest. Ransom (24) recorded the presence of distended abdominal veins in 4 of his 16 cases.

In none of the 16 cases of carcinoma of the head of the pancreas were distended abdominal veins observed.

Enlargement of Liver and Spleen. The liver was more or less easily palpable in 11 of the 16 cases of carcinoma of the body or tail of the pancreas. In 4 cases the liver was described as hard and nodular or irregular; in 5 other cases it was said to be hard or firm but apparently smooth, and in the 2 remaining cases the edge of the liver was palpable but no further comment was recorded. In 4 cases the spleen was enlarged and definitely palpable.

Among the 16 cases of carcinoma of the head of the pancreas, the liver was palpable in 12, but it was described as nodular in only 1 case. In none of the cases could the spleen be felt.

Jaundice. In 8 of the 16 cases of carcinoma of the body or tail of the pancreas a slight degree of jaundice of the sclerae or skin appeared shortly before the fatal termination of the disease. In 2 cases jaundice was first noticed a month prior to death but in one of these it varied considerably in intensity, even disappearing completely for a few days. In the remaining 6 cases jaundice appeared less than 2 weeks before death. The jaundice was slight in every case except one in which faint jaundice rapidly became more intense until death 8 days later. In none of these cases was the jaundice associated with palapable enlargement of the gall bladder nor was there any note of lack of pigment in the stools.

Among the 16 cases of carcinoma of the head of the pancreas, jaundice, frequently accompanied by clay coloured stools, was recorded as one of the initial complaints in 13 cases and it persisted or became deeper until death, or until it was relieved by cholecystgastrostomy. In 6 of these cases the gall bladder became palpably enlarged. In 3 cases there was never any jaundice during the whole course of the illness.

Palpable Tumour Masses. In 2 of the 16 cases of carcinoma of the body or tail of the pancreas an epigastric tumour mass was palpable. In one of these cases a firm, smooth, tense mass, toward the right side of the epigastrium, extended to the umbilicus. In the other case a firm nodular mass in the mid-epigastrium was thought to be connected with the liver. In the latter case were also numerous subcutaneous nodules and a distinct rectal shelf. Two additional cases had umbilical tumour nodules. In a fifth case an enlarged supraclavicular lymph node was removed four days before death and diagnosed pathologically as secondary adenocarcinoma.

X-ray Findings. X-ray examinations were carried out in 10 of the 16 cases of carcinoma of the body or tail of the pancreas. The examination consisted of a gastric series in 2 cases, a barium enema in one case, and both types of examination in 7 cases. In 6 cases the results were completely negative. In 3 cases although no lesions could be made out in the gastro-intestinal tract itself, distortion of the shadows suggested generalized peritoneal tumour metastases in one case, a mass in the right upper quadrant of the abdomen in another, and in the third case, a mass pressing on the greater curvature of the stomach from without. In one case there was some retention of barium in the

TABLE II

Misleading signs and symptoms in carcinoma of the body or tail of the pancreas

CASE	ASCITES DURATION PRIOR TO DEATH	HEMATEMESIS (NUMBER OF OCCASIONS)	BLOOD IN STOOLS	DISTENDED ABDOMINAL VEINS	PALPABLE SPLEEN	PALPABLE LIVER	JAUNDICE (DURATION PRIOR TO DEATH)
	weeks						
1	0	0	0	0	0	Firm and smooth	0
2	3	0	0	0	Present	Firm	0
3	5	Bloody vomitus (1)	0	Present	0	Hard and nodular	Slight (5 days)
4	0	0	0	0	0	Firm and tender	Slight (11 days)
5	0	Clotted blood (1)	0	0	0	Firm and tender	0
6	3	0	Guaiac positive	0	0	0	Slight (13 days)
7	0	Coffee-ground vomitus (2)	Guaiac positive	0	0	0	0
8	4	Repeated hematemeses	0	0	0	0	0
9	2½	0	Guaiac positive	0	0	0	0
10	0	Frequently repeated hematemeses	Tarry stools	0	Present	Edge felt	0
11	17	Large amount of blood (1)	Clots of blood, tarry stools	0	Present	Hard and irregular	Slight scleral (9 days)
12	2	0	Tarry stools	0	0	Edge felt	Slight—Fluctuating (30 days)
13	0	Blood streaked (1) old blood and clots (1)	0	0	0	Firm and irregular	Slight (30 days)
14	11	0	0	0	Present	Large and hard	Slight to deep (8 days)
15	2	0	0	0	0	0	Slight (11 days)
16	6	Blood (1)	0	Present	0	Firm and nodular	0

0 = Absent or not recorded.

oesophagus and a large filling defect in the proximal third of the stomach suggesting a malignant growth.

Similar examinations were made in 10 of the 16 cases of carcinoma of the head of the pancreas with negative results in 4 cases. In 4 other cases, however, the X-ray findings were interpreted as indicating the presence of a tumour mass pressing upon or invading the pylorus or duodenum from without, and in 2 additional cases there was evidence of an obstructive lesion at the pylorus.

Duration of Illness. Among the 16 cases of carcinoma of the body or tail of the pancreas, the shortest duration of the illness from the onset of definite symptoms to death was 7 weeks and the longest was 19 months. In 10 cases the duration was between 2 and 5 months. The average duration of all cases was slightly over 5 months, but omitting the one case of 19 months duration the average was 4.2 months.

Among the 16 cases of carcinoma of the head of the pancreas, the shortest duration of the illness was 6 weeks and the longest 12 months. In 11 cases the duration was between 3 and 6 months and the average duration of all cases was 4.6 months.

Recorded Clinical Diagnoses. The clinical diagnosis of carcinoma of the body or tail of the pancreas is extremely difficult. In the present series of cases the correct diagnosis was not made in a single instance in spite of the fact that exploratory laparotomy was carried out in four of them. In Ransom's series (24) a correct pre-operative diagnosis was made in only 3 of the 16 cases. In his series the commonest erroneous diagnosis was carcinoma of the colon. In the present series the same was true. Carcinoma of the colon was the diagnosis in 4 cases, carcinoma of the stomach in 3 cases and secondary carcinoma of the liver of undetermined origin in 4 cases. One case was diagnosed as carcinoma of the gall bladder on the basis of findings at laparotomy. Among the 4 remaining cases, a diagnosis of malignant tumour was rejected in favour of cirrhosis of the liver in 2 cases, syphilis of the liver in one case and an inflammatory obstructive lesion of the colon in one case.

PATHOLOGICAL FEATURES

So far as the primary tumours are concerned, carcinomata of the body or tail of the pancreas differ in no essential respect from those which originate in the head.

The primary growth forms a firm, sometimes nodular mass within the pancreas, but it may not be large enough to bulge appreciably on the surface and, when such a tumour occupies the tail, there may be scarcely any distortion of the general contour of the organ. However, if the tumour is located in the body, the tail is shrunken and indurated due to obstruction of the pancreatic duct. The larger tumour masses are formed partly by growth of the neoplasm within the pancreas but far more by direct invasion of contiguous structures and involvement of neighbouring lymph nodes so that the pancreas is matted in a mass of tumour tissue most of which is really outside the limits of the pancreas itself. A large mass formed in this way develops not infrequently around a primary carcinoma of the body or tail of the pancreas and this fact probably explains the statement of Kiefer (17) and others that the larger tumours have their origin in the body or tail of the pancreas rather than in the head.

The consistency and gross appearance of the primary growth depend, of course, upon the degree of cellularity of the tumour and the abundance of the stroma. In most instances the tumour mass is scirrhous, stony-hard, almost gritty to the knife-edge and fibrous in appearance, but occasionally it is medullary in character with a soft consistency and a fleshy cut surface which may present more or less extensive, irregular, yellowish areas of necrosis contrasting with the greyish background of intact tumour tissue. In a very few cases the tumour has a gelatinous mucoid character, or it may be riddled with small or large cystic spaces filled with mucoid material.

Histological Types. Carcinomata of the pancreas in general occur in three main histological forms. By far the most frequent is the cylindrical cell adenocarcinoma originating from the epithelium of the pancreatic duct system and consisting of irregular duct-like spaces lined by cuboidal or columnar epithelial cells in a layer one or several cells deep. In some instances these cells show a marked tendency to form small papillary projections into the lumen (Fig. 1). The individual cells have clearly defined margins and possess a vesicular nucleus usually with a single nucleolus. The tumours in which columnar cells predominate usually show well formed tubular spaces and a dense fibrous stroma, but those made up largely of cuboidal cells often present great numbers of small poorly formed acini and small solid clusters or narrow strands of anaplastic cells, sometimes with giant or multiple nuclei, strewn through a stroma which is only moderately dense (Fig. 2). Tumours of this cylindrical cell type are almost always scirrhous but if the stroma is scanty their gross appearance may approach that of a medullary tumour.

A much less common form of pancreatic carcinoma is the acinar cell cancer in which the type cell resembles those of the parenchyma of the pancreas. It consists of lobular masses of polyhedral or rounded cells with poorly defined cell margins and large hyperchromatic nuclei in which nucleoli are inconspicuous or absent. In some instances, well differentiated cells closely resembling those of the pancreatic parenchyma form fairly regular rows (Fig. 3) or small, rounded clusters reminiscent of pancreatic acini. In other cases, however, there is no

special arrangement of the cells which are, for the most part, small and rounded but which may display pleomorphic tendencies in the formation of spindle shaped cells or large cells of bizarre shapes with giant or multiple nuclei (Fig. 4). Marked pleomorphism may render the tumour difficult to distinguish from a sarcoma. The stroma of these tumours is delicate and the gross consistency is correspondingly soft.

The third histological type, the islet-cell carcinoma of the pancreas, is rare. It is true that Fabozzi (8) stated many years ago that almost all carcinomata of the pancreas originated from the islets of Langerhans, but this statement has never been accepted, though none can deny that Fabozzi possibly did observe some cancers of this type. In any event, the occurrence of carcinomata composed of cells simulating in form or function those of the islets of Langerhans was not brought to general recognition until 1927 when Wilder and others (31) reported a case in which the tail and part of the body of the pancreas were occupied by a tumour of this character which had metastasized to the neighbouring lymph nodes and liver. In their case the tumour cells were functional and the patient suffered from hyperinsulinism. Only 6 other cases of this type of pancreatic carcinoma have been reported in the interval (4, 6, 7, 11, 16, 32), and 3 of the 6 patients had hyperinsulinism. Among the 50 cases of carcinoma of the pancreas from which the material for the present study was drawn, only one tumour of this type was encountered. It involved the whole pancreas diffusely and had metastasized to the regional lymph nodes, liver, peritoneum, pericardium, thyroid, adrenals, kidney glomeruli and vertebrae. In two other unreported cases which I have had the opportunity of studying, the tumour also occupied the whole pancreas and there were widespread metastases. In none of these cases was there any clinical evidence of disturbance of carbohydrate metabolism. The tumours in these three cases, in common with those previously described, consisted of cells strikingly similar to those of normal islets of Langerhans. The tumour tissue was made up of rounded infiltrating masses of cells arranged in narrow strands and small clusters supported by ramifying fibrous bands which composed the stroma (Fig. 5). In some of the reported cases, however, the tumour cells were arranged in more solid masses, or even interspersed in narrow rows between dense, broad bands of fibrous stroma. These tumours, accordingly, have varied in gross consistency from soft to firm or even hard.

While carcinomata of all three histological types may originate in the body or tail of the pancreas as well as in the head, it happened in the present series that the tumours in 14 of the 16 cases of carcinoma of the body or tail of the pancreas and in all of the 16 comparative cases of carcinoma of the head of the pancreas were of the cylindrical duct-cell type. The remaining two cases of carcinoma of the body or tail of the pancreas were of acinar cell type.

With respect to *the spread of carcinoma of the pancreas*, a marked difference exists between primary carcinoma of the head of the pancreas and carcinoma arising in the body or tail, in that the latter tends to extend much more massively and to metastasize more widely. Of course, it is not to be inferred that massive and widespread dissemination of the tumour occurs in every case of carcinoma of the body or tail of the pancreas. Among the 16 cases analyzed here, however, only one was free from metastases, 2 cases had metastases limited to the regional lymph nodes and liver, while in the remaining 13 cases the tumour had spread beyond these limits to various other tissues and organs. Among the 16 cases of carcinoma of the head of the pancreas, there were 4 cases in which no metastasis had occurred and 9 cases in which the tumour had not spread beyond the regional lymph nodes and liver. In only 2 cases was there a really wide distribution of tumour metastases. The organs and tissues secondarily involved in these cases of cancer of the pancreas and the frequency of involvement of each are shown in Table III in which primary carcinoma of the body or tail of the pancreas is contrasted with carcinoma arising in the head. While this table shows the frequency with which the various organs are involved it gives no indication of the fact, to be referred to in greater detail presently, that the involvement especially of the peritoneum, abdominal lymph nodes and liver, tends to be much more massive in association with primary carcinoma of the body or tail of the pancreas than with carcinoma of the head of that organ.

The spread of carcinoma of the pancreas, whether originating in the head, body or tail, is by direct extension into neighbouring tissues and by way of perineural spaces, lymphatics and blood channels, especially veins. With respect to extension by way of perineural spaces, there is little difference between carcinomata arising in the head and those arising in the body or tail of the pancreas. But the opportunities for both local and distant spread by direct extension and *via* blood channels are much greater in the case of carcinoma of the body or tail than of carcinoma of the head of the pancreas, as I shall attempt to show in subsequent paragraphs.

Growth of the tumour along nerve sheaths (Fig. 6) is probably not of great importance in furthering spread to distant sites, but this process acquires significance in the explanation of the deep seated, gnawing

abdominal pain which is so common as a clinical manifestation of cancer of the pancreas. Since the posterior surface of the body of the pancreas lies directly upon the coeliac plexus and immediately adjacent to the nerves entering and emerging from it, there is good reason to suppose that the chances in favor of involvement of these nerves by tumour would be greatest in the case of carcinoma originating in the body of the pancreas. This was suggested years ago by Chauffard

TABLE III

Spread of carcinoma of pancreas. Frequency of involvement of various organs and tissues

ORGANS AND TISSUES SECONDARILY INVOLVED	PRIMARY IN BODY OR TAIL, 16 CASES	PRIMARY IN HEAD, 16 CASES
Liver	13	9
Abdominal lymph nodes	10	9
Peritoneum	12	2
Lung	6	2
Pleura	6	0
Diaphragm	5	0
Adrenal	4	1
Kidney	3	0
Vertebrae	3	0
Stomach	3	0
Colon	3	0
Mediastinal and peribronchial lymph nodes	3	0
Pericardium	2	0
Spleen	2	1
Gall bladder	2	0
Umbilicus	2	0
Subcutaneous tissues	1	0
Supraclavicular lymph node	1	0
Ureter	1	0
Ovaries	1	0
Duodenum	0	3

(5) as the explanation of the unusual severity of the abdominal pain in his cases of carcinoma of the body of the pancreas. There is no doubt, however, that invasion of nerve sheaths does occur in carcinoma of the head or tail of the pancreas, as I have observed repeatedly in microscopical sections of such tumours, but it is probable that fewer and smaller nerves are involved than in carcinoma of the body of the pancreas.

The direct extension of carcinoma of the pancreas originating in the head is, for the most part, obstructed by surrounding structures. The position of the pancreas against the posterior wall of the abdomen prevents massive extension in the posterior direction. It is the rule to find the lower end of the bile duct surrounded and compressed to the point of occlusion by the tumour mass, but it is seldom that any other important structure posterior to the head of the pancreas is invaded. The head is surrounded on three sides by the duodenum and is buried effectively beneath the proximal part of the transverse colon from which it is separated by loose areolar tissue. Both the duodenum and colon are resistant to invasion and they tend to block the advance of the tumour. The duodenum, lying in close contact with the head of the pancreas, may sometimes be compressed or invaded, but only occasionally does the tumour penetrate to the lumen. The local extension of cancer of the head of the pancreas is thus rather sharply restricted by the anatomical arrangement of adjacent structures and, presumably for this reason, the primary tumour mass is usually confined almost entirely to the pancreas and is relatively small. The head of the pancreas is in contact with the peritoneum only in one small area toward the lower margin of the anterior surface. It is only in a few cases that carcinoma arising in the head of the pancreas reaches this particular spot and extension by peritoneal implantation is correspondingly rare. When this does occur, the peritoneal metastases are usually small and sparsely distributed.

All of this is in marked contrast to the excellent opportunities for direct extension which exist when the primary tumour originates in the body or tail of the pancreas. In the posterior direction, it is true, the way is blocked by the left crus of the diaphragm, the left adrenal, left kidney and spleen. The adrenal gland is sometimes invaded but the capsules of the kidney and spleen are resistant to invasion and these organs are seldom involved by direct extension of the tumour. On the other hand, the anterior and inferior surfaces of the body and tail of the pancreas are covered only by peritoneum. The anterior surface faces the lesser sac of the peritoneum, while the inferior surface faces the general peritoneal cavity, the two being separated by the transverse mesocolon. The body and tail of the pancreas are more slender than the head, and no point in the interior is very far removed

from the investing peritoneum. Thus, direct spread of the cancer to either peritoneal surface occurs readily and frequently, with consequent massive and widespread peritoneal implantations. So, too, direct extension along peritoneal surfaces or massive growth of the primary tumour may lead to involvement of the transverse colon, stomach or diaphragm. These structures are not often completely penetrated, but extension to the lumen of the stomach or colon occasionally occurs with consequent ulceration. The transverse colon, however, may be encircled and constricted by tumour without significant penetration of its walls. Permeation of the diaphragm may lead to involvement of the pleura, or, less frequently, the pericardium, with the production of multiple pleural or pericardial implantations. It seems evident that this marked tendency of carcinoma of the body or tail of the pancreas to spread so widely in various directions by direct extension is dependent upon the anatomical position and relations of these portions of the pancreas.

Extension of carcinoma of the pancreas by way of lymphatic channels to adjacent lymph nodes occurs with about the same frequency in carcinoma of the head of the pancreas as in carcinoma of the body or tail. But lymph node metastases from carcinoma of the head of the pancreas, when they occur, are usually confined to the nodes of the subpyloric group which are clustered around the head of the pancreas. On the other hand, carcinoma of the body or tail of the pancreas frequently spreads not only to the immediately adjacent lymph nodes of the pancreatico-lienal group but much more widely to involve the gastric, hepatic, coeliac, mesenteric and peri-aortic groups and even the mediastinal and peribronchial lymph nodes. No obvious anatomical explanation of this difference is provided even by the comparatively lucid description of the lymphatic drainage of the pancreas to be found in Rouvière's recent monograph on the lymphatics in man (26). In the lack of an explanation based on the anatomy of the lymphatics of the pancreas, one can only suggest the possibility that the wider lymphatic spread of carcinoma of the body or tail of the pancreas is really dependent on the more extensive spread of these tumours by direct invasion of surrounding tissues. During the course of this direct extension it may well be that lymph channels are invaded which lead to groups of lymph nodes not directly concerned with the

lymph drainage of the pancreas itself. Such an occurrence would readily account for a rather massive involvement of lymph nodes anywhere in the neighbourhood of the primary growth. In any event, no better theory presents itself in explanation of the observed fact that carcinoma of the body or tail of the pancreas, as compared with carcinoma of the head, tends to spread much more widely among the various groups of lymph nodes in the upper abdomen and even beyond this region.

As to the rôle of the thoracic duct in the spread of pancreatic cancer, no information was obtained in the present study beyond the fact that in one case of carcinoma of the body of the pancreas one of the left supraclavicular lymph nodes was involved by the tumour, an occurrence which is said to indicate spread of cancer by way of the thoracic duct. A few cases of carcinoma of the pancreas associated with chylous ascites are to be found in the literature but none was encountered among the cases which are analyzed here.

Metastasis by way of blood channels from primary carcinoma of the pancreas, whether of the head, body or tail, occurs most frequently to the liver *via* the portal vein. The metastases in the liver arising from carcinoma of the head of the pancreas may consist of a few small nodules or there may be many such nodules, but really massive involvement of the liver is not a frequent occurrence. In none of the 16 cases of carcinoma of the head of the pancreas analyzed here could the metastases in the liver be described as very massive and in none of the cases did the weight of the liver exceed 2500 grams. On the other hand massive metastatic involvement of the liver is common in cases of carcinoma of the body or tail of the pancreas. The livers in 6 of the 16 cases of the present series were almost completely occupied by metastatic tumour masses and weighed from 2500 to 3900 grams. There is an obvious and adequate anatomical explanation of this marked difference between carcinoma of the head and carcinoma of the body or tail of the pancreas.

The head of the pancreas is drained by veins of relatively small size, while the body and tail are drained by short venous channels into a large vein, the splenic, which lies in intimate relation partly embedded in a groove running along the upper margin of these portions of the pancreas. Although the invasion of small veins by carcinoma

may lead to hematogenous dissemination of the tumour, it is probable that such veins are soon plugged either by tumour tissue or by the formation of thrombi. The growth of tumour into the lumen of a large vein, on the other hand, is much more likely to lead to the development of massive blood-borne metastases since the passing blood stream may be heavily seeded with tumour cells for some time before complete occlusion of the vein occurs. The high probability of invasion of the splenic vein by carcinoma of the body or tail of the pancreas, therefore, provides a perfectly plausible explanation of the much greater tendency of these tumours to metastasize massively to the liver. Unfortunately, the splenic vein is not always examined carefully at autopsy nor specifically mentioned in autopsy protocols. In the protocols of the 16 cases of carcinoma of the body or tail of the pancreas in the present series, the splenic vein is mentioned in only 6 cases, but it is significant that among these 6 cases in which the splenic vein was examined at autopsy it was found to be invaded by the tumour and occluded by tumour tissue or thrombosis in 5 cases, and normally patent in only one (Fig. 7).

In none of the cases of carcinoma of the body or tail of the pancreas was there recorded any unequivocal evidence of gross portal embolism either by fragments of tumour tissue or thrombus material. The findings in the cases with metastases in the liver suggested a diffuse seeding of the organ with tumour cells brought by way of the portal blood stream. In many of the cases it was possible microscopically to find plugs of tumour cells filling fine radicles of the portal vein within the liver (Fig. 8). In the cases with massive metastases in the liver it appeared in microscopical sections that almost all of the portal radicles were plugged in this way. If such a condition existed throughout the liver, the obstruction to the portal circulation must have been serious, but the importance of this potential cause of portal obstruction is difficult to assess since it is obviously impossible to examine the whole liver microscopically. Nevertheless, it would appear reasonable to suppose that the plugging of intrahepatic radicles of the portal vein might reach such proportions that it could seriously impede the portal circulation.

Obstruction of the portal circulation may also occur in other ways. Large tumour nodules in the liver may compress or invade the main

intrahepatic branches of the portal vein and this may be followed by thrombosis of these large branches or even of the portal vein itself. Large intrahepatic branches of the portal vein were grossly occluded in this way in 3 of the 16 cases of carcinoma of the body or tail of the pancreas and there was thrombosis of the main portal vein in one case. In 3 cases the portal vein was markedly compressed at the porta hepatis by matted masses of lymph nodes enlarged by metastatic tumour. Bile channels may also be obstructed either by intrahepatic metastases pressing upon large bile ducts within the liver or by secondary extrahepatic tumour masses compressing the ducts as they emerge from the porta hepatis.

From the liver, the tumour may spread farther by way of blood channels to the lungs. This occurred in 6 of the 16 cases of carcinoma of the body or tail of the pancreas. Still more widespread blood-borne metastases in the adrenals, kidneys, spleen or vertebrae were found in 5 cases, all of which had tumour involvement of the lungs or pleura or both, indicating that the pulmonary circulation was probably the point from which this tertiary blood stream dissemination had occurred.

Before concluding this discussion of the spread of cancer of the pancreas, it may be well to anticipate the possible suggestion that the greater tendency of carcinoma of the body or tail of the pancreas to spread widely is dependent not so much upon the anatomical opportunities for extension as upon longer survival of the patient after the initiation of malignant changes in the pancreas. While one cannot deny this possibility, there is no evidence to support the idea. Reference to the section of this paper dealing with the clinical features of the disease will show that among the cases analyzed there was no significant difference in the duration of life following the onset of the earliest symptoms between the group of cases of carcinoma of the body or tail of the pancreas and the cases of carcinoma of the head. It is possible that carcinoma of the body or tail of the pancreas may remain clinically "silent" longer than carcinoma of the head, but the unproved assumption that this does occur can scarcely be accepted in explanation of the greater tendency of carcinoma of the body or tail of the pancreas to spread widely, especially when adequate reasons for this are to be found in the anatomical relations of the body and tail of the pancreas as compared with the head.

RELATION OF SIGNS AND SYMPTOMS TO THE SPREAD OF CARCINOMA OF THE BODY OR TAIL OF THE PANCREAS

A knowledge of the various modes and directions of spread of carcinoma of the body or tail of the pancreas which have been described in the preceding part of this paper renders it relatively easy to understand the occurrence of certain rather unexpected and misleading clinical signs and symptoms which are encountered not infrequently in this disease. The production of some of the signs and symptoms requires no special discussion here, but brief comment may be made on the origin of others. I have discussed in detail elsewhere (12) the production of the signs and symptoms in one case of the present series (Case 11, carcinoma of the tail of the pancreas).

Abdominal Pain. In explanation of the paroxysms of severe abdominal pain, the suggestion of Chauffard (5) that it is due to involvement of nerves of the coeliac plexus seems the most probable, although it is difficult to understand why the pain should occur in intermittent attacks. The same explanation applies even more plausibly to the constant, dull, boring or aching, mid-epigastric pain which occurred in 10 of the 16 patients in the present series. Afferent nerve fibres within the pancreas itself are probably affected first, but posterior extension of the tumour would almost surely result in pressure upon or invasion of the sympathetic nerves leading to other abdominal organs with consequent irritation of the afferent fibres accompanying them and the production of more severe pain. This probable course of events corresponds with the increasing severity of the constant abdominal pain during the course of the disease and with the increasing frequency and severity of the intermittent attacks of paroxysmal pain. Somatic sensory nerves supplying the posterior parietal peritoneum and the retroperitoneal tissues may also be involved and this may explain the occurrence of pain in the sides and back. The intermittent attacks of severe colicky abdominal pain which occurred in 4 of the 16 patients were probably due to partial intestinal obstruction since in all of these cases there was found at autopsy either invasion or constriction of the intestine by peritoneal tumour masses which could easily have produced partial obstruction of the intestinal lumen.

Ascites. The presence of fluid in the abdomen was detected clinically in 10 of the 16 cases of carcinoma of the body or tail of the pan-

creas. The autopsy findings in these cases made it clear that the development of ascites was determined either by the presence of carcinomatosis of the peritoneum or by obstruction of the portal circulation or by the concomitant influence of both of these factors. Widespread peritoneal tumour implants were found in 8 of the 10 cases with ascites, and in 2 of these 8 cases there was also gross obstruction of the portal circulation produced in one case by thrombosis of the portal vein and in the other by compression of the portal vein by metastatic tumour masses at the porta hepatis. The 2 remaining cases in which ascites occurred lacked peritoneal tumour implants but in both cases there was gross portal obstruction. In one case the portal vein was surrounded and markedly compressed by a mass of tumour at the hilum of the liver, while in the second case the large intrahepatic branches of the portal vein were compressed and grossly invaded by tumour nodules in the liver. No account can be taken here of the theoretical possibility of serious obstruction of the portal circulation produced through the plugging of minute intrahepatic radicles of the portal vein by tumour cells, although there were several cases in which gross and microscopic examination of the liver suggested that this process may well have been sufficiently extensive throughout the liver to have constituted an important factor in the production of ascites.

Hematemesis and Blood in the Stools. In cases of carcinoma of the body or tail of the pancreas, hematemesis or the appearance of blood in the stools may follow haemorrhage into the stomach, intestine or rectum from sources of two kinds. The stomach or intestine may be invaded by the pancreatic tumour or by peritoneal implants with consequent ulceration and bleeding; or obstruction of the portal circulation may lead to engorgement, dilatation and finally rupture of veins at the lower end of the oesophagus or in the cardiac end of the stomach or in the rectum.

Hematemesis occurred in 8 of the 16 cases in the present series. Carcinomatous invasion of the stomach was the cause of the bleeding in 2 cases, while in 6 cases the autopsy findings were such as to justify the assumption that bleeding into the stomach was the result of portal obstruction, although the actual point of bleeding from dilated veins in the oesophagus or stomach was found in only 2 cases.

Tarry stools were observed or occult blood detected in the stools in 3 of the cases in which hematemesis had occurred and in 2 of these cases there was no source of bleeding other than that which had led to hematemesis. In one case, however, clots of fresh blood were passed *per rectum* in addition to tarry stools. This was explained by the presence of haemorrhoids from which the patient had suffered for years, but the gross rectal bleeding may well have been precipitated by portal obstruction caused in this case by thrombosis of the portal vein. In one case in which hematemesis did not occur, tarry stools were the result of carcinomatous invasion of the intestine with ulceration. In 2 cases the recorded autopsy findings failed to explain the presence of occult blood in the stools.

Enlargement of the Spleen. While splenic metastases from carcinoma of the body or tail of the pancreas might cause gross enlargement of the spleen, this appears to be rare. The most frequent cause of splenomegaly in this disease is obstruction of the portal circulation or of the splenic vein or of both. Clinical examination revealed an enlarged spleen in 4 of the 16 cases in the present series. The weights of the spleens at autopsy in these cases were 250, 300, 500 and 500 grams, respectively. In one other case the spleen was found at autopsy to be enlarged, weighing 260 grams, but in all of the remaining cases it was within normal limits of size or smaller than normal. Of the 5 enlarged spleens, 2 contained tumour metastases but these were not of sufficient size to account for the splenic enlargement. The splenomegaly was explained in 2 of the 5 cases by gross portal obstruction, in one case by occlusion of the splenic vein without portal obstruction, and in one case by complete occlusion of both splenic and portal veins. In the one remaining case neither the splenic or portal veins were described in the autopsy protocol. It is possible that complete or partial occlusion of one or both of them could have been overlooked in the post mortem examination.

In 5 cases of the present series the spleen was found at autopsy to be of normal size or smaller than normal in spite of the presence of gross portal obstruction in 2 of these cases and occlusion of the splenic vein in the remaining 3 cases. There are two possible explanations of this apparent discrepancy. It seems reasonable to suppose that the

occurrence of splenic enlargement as a result of obstruction of the splenic or portal veins depends, at least in part, upon the rapidity with which the obstruction is produced and also upon the rapidity of development of an adequate collateral circulation. If the venous obstruction developed gradually and if collateral circulation could compensate for the obstruction, enlargement of the spleen might fail to make its appearance. On the other hand, enlargement of the spleen produced by a relatively sudden obstruction of the venous outflow may not be permanent. It is possible that the subsequent development of an adequate collateral venous drainage may permit a reduction in the size of the spleen in the course of time to normal or less than normal dimensions, as occurs in experimental animals in which the portal or splenic vein is obstructed (22, 30).

Enlargement of the Liver. Every instance of enlargement of the liver among the cases in the present series was adequately explained by the finding at autopsy of more or less massive metastatic tumour involvement of the liver.

Jaundice. The occurrence of jaundice as a terminal development in 8 of the 16 cases of carcinoma of the body or tail of the pancreas was found at autopsy to be due to compression and obstruction of the large bile ducts within the liver by intrahepatic tumour nodules, or the result of compression of the bile ducts emerging from the porta hepatis by extrahepatic masses of metastatic tumour located at the hilum of the liver.

SUMMARY

Sixteen unselected cases of primary carcinoma of the body or tail of the pancreas with adequate clinical and autopsy records are analyzed from both the clinical and pathological points of view with the object of calling attention to the tendency of cancer of the pancreas originating in the body or tail to spread in such a way as to produce clinical signs and symptoms not hitherto recognized as common in this disease.

The most constant symptoms are those emphasized by previous writers, namely, severe abdominal pain and marked loss of weight, but other important signs and symptoms of a rather misleading char-

acter are recorded in a large proportion of the cases in the present series. Ascites occurred in 10 of the 16 cases and hematemesis in 8 cases. Occult or gross blood was observed in the stools in 6 cases. The spleen was palpably enlarged in 4 cases and the liver in 11 cases. Slight jaundice appeared terminally in 8 cases.

An account of the pathological features of carcinoma of the pancreas in general is followed by a description of the various modes and directions of spread of cancer of the body and tail of the pancreas based upon the autopsy findings in the 16 cases studied. Comparison with the autopsy findings in 16 consecutive cases of carcinoma of the head of the pancreas shows that primary cancer of the body or tail of the pancreas tends to spread much more widely and massively than carcinoma originating in the head. An adequate explanation of this tendency is afforded by a consideration of the anatomical position and relations of the body and tail as contrasted with the head of the pancreas.

Direct extension of carcinoma of the body or tail of the pancreas frequently leads to widespread involvement of the peritoneum and sometimes to invasion of the stomach or intestines. The abdominal lymph nodes are often massively involved. Invasion of the splenic vein with the consequent occurrence of massive metastasis to the liver may be followed by occlusion of the splenic vein, obstruction of large intrahepatic branches of the portal vein or even occlusion of the portal vein itself.

These pathological developments in carcinoma of the body or tail of the pancreas are responsible for the appearance of the various clinical signs and symptoms already mentioned. Brief comment is made upon the production of each of these.

The author is much indebted to Dr. Anne M. Bahlke for valuable assistance in the collection of the clinical data used in this paper.

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PLATE 1

FIG. 1. CARCINOMA OF THE PANCREAS OF WELL DIFFERENTIATED DUCT-CELL TYPE

Showing irregular duct-like structures with papillary ingrowths of the lining epithelial cells. × 120.

FIG. 2. CARCINOMA OF THE PANCREAS OF UNDIFFERENTIATED DUCT-CELL TYPE

Several multinucleated cells are shown. × 240.

FIG. 3. CARCINOMA OF THE PANCREAS OF WELL DIFFERENTIATED ACINAR CELL TYPE

The cells resemble the parenchymal cells of the pancreas and are arranged in more or less regular rows. × 240.

FIG. 4. CARCINOMA OF THE PANCREAS OF ANAPLASTIC ACINAR CELL TYPE

There is no regularity of arrangement and the cells vary greatly in size and shape. Several cells with giant nuclei are shown. × 240.

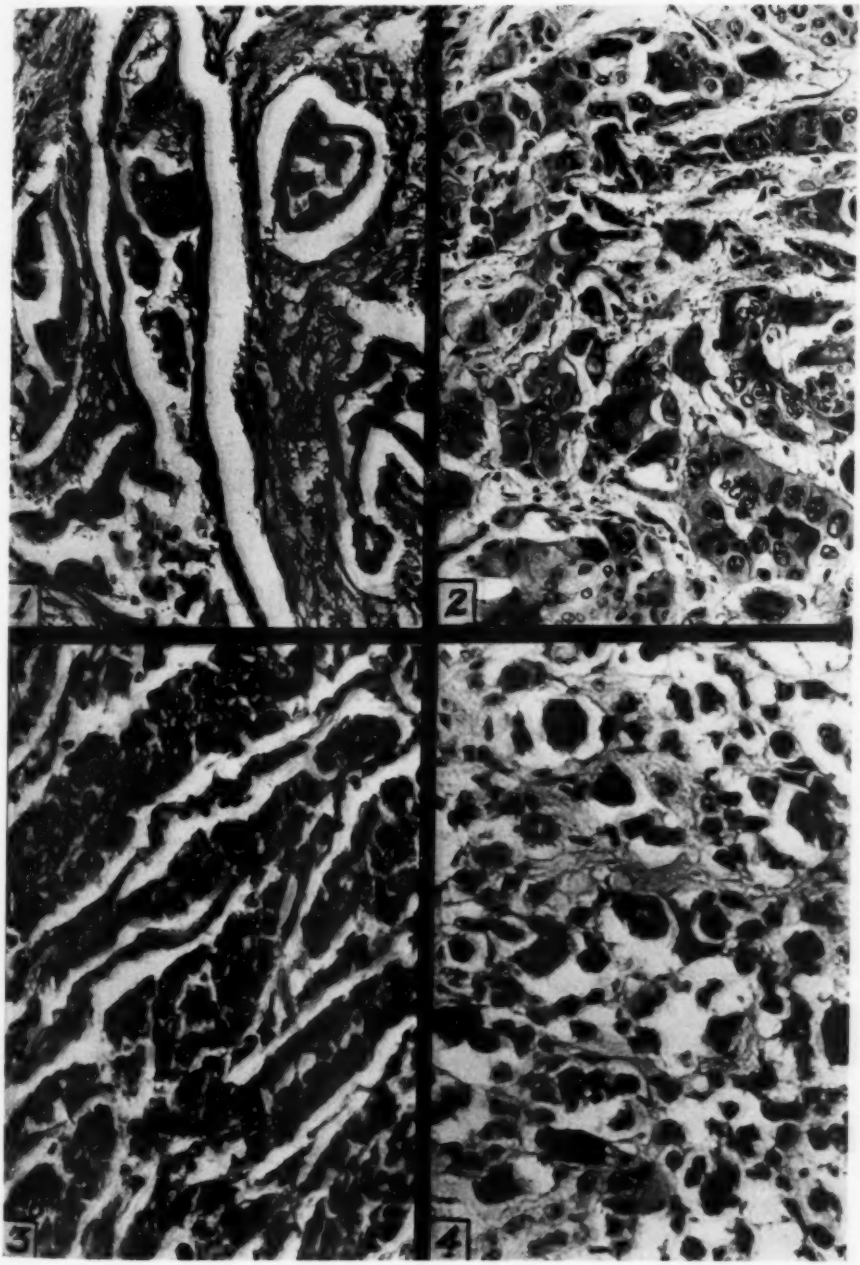
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Plate 2

Fig. 5. Islet-Cell Carcinoma of the Pancreas

Note the striking resemblance to normal islets of Langerhans both in the appearance of individual cells and in their general arrangement. × 240.

Fig. 6. Sympathetic Nerves in the Vicinity of the Pancreas Compressed and Distorted by the Spread of Pancreatic Carcinoma along the Perineural Spaces

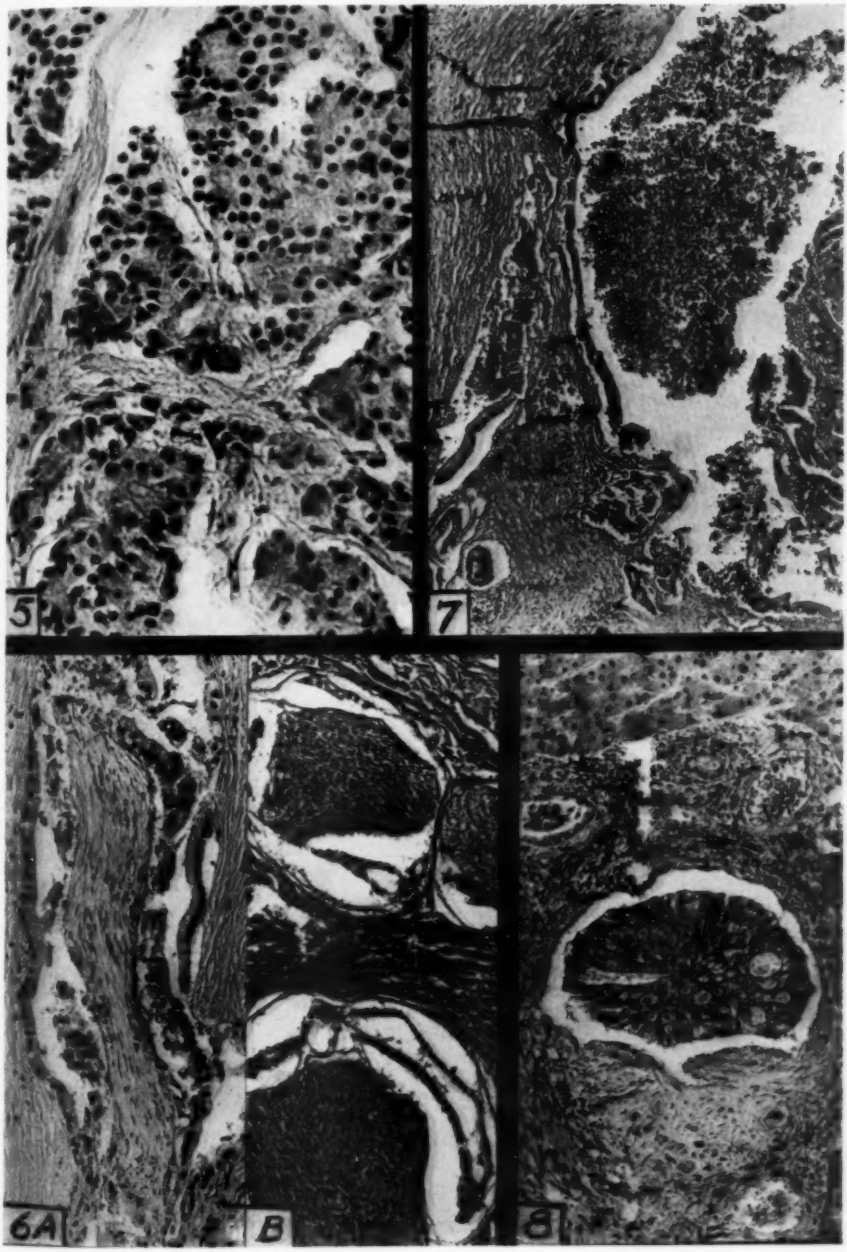
(*A*) Nerve cut longitudinally. (*B*) Nerves cut transversely. × 75.

Fig. 7. A Segment of the Wall of the Splenic Vein under Low Magnification Showing Invasion of the Wall by Carcinoma of the Body of the Pancreas

Tumour cells have reached the lumen where they form a partial lining and also lie strewn amongst blood cells and small masses of thrombus material. × 45.

Fig. 8. A Portal Area of the Liver in a Case of Carcinoma of the Body of the Pancreas

A plug of tumour cells occupies the lumen of the portal venule and some extension has occurred into the adjacent tissue. × 75.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A PHYSIOLOGICAL STUDY OF THE MOVEMENTS IN PALATAL MYOCLONUS

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Myoclonus of the soft palate was first described by Politzer; Spencer in 1886 discussed the abnormality under the name of pharyngo-laryngeal nystagmus. There have been several reports of clinical cases; search of the literature revealed over fifty articles most of them written by French neurologists, particularly by Foix and his pupils.

Palatal myoclonus is a syndrome dependent on injury of definite structures in the nervous system; it is usually caused by vascular accidents, and for this reason is found most commonly in elderly people. It may be produced in young individuals by any disease process which injures the central tegmental fasciculus, inferior olivary nucleus or possibly the dentate nucleus. Similar movements are seen in certain patients with sequelae of lethargic encephalitis.

The motor disturbance sometimes involves the soft palate alone but frequently the abnormal movements are also observed in the muscles of the face, soft palate, buccal floor, pharynx, larynx, intercostal muscles and diaphragm. Hence the name of palatal myoclonus is scarcely descriptive of the syndrome. Occasionally movements of the eyes have been included. Speech is abnormal due both to the myoclonic movements and to the associated destruction of cerebellar pathways. The rhythm of the myoclonus is usually described as regular. The movements are said to continue during sleep, although they are decreased in amplitude. They persist under anesthesia.

Leshin and Stone (1932) were of the opinion that the movements usually have two phases, rapid and slow. Those of the soft palate are in a vertical plane, if both sides are involved equally. The posterior faucial pillars in cases of bilateral involvement approach one another in the midline and then return to their normal positions. The vocal cords and arytenoids are in continuous motion; the ampli-

tude occupying usually from one-third to two thirds their normal excursion. The rate is synchronous with that seen in the palate and pharynx.

Our observations were made upon the following case.

CASE REPORT

Patient of 34 years with obscure disease of the nervous system progressing for seven years, with left peripheral facial palsy, right hemiparesis, loss of emotional expression on right side of face, emotional instability, loss of abdominal reflexes, synchronous rhythmical movements of the soft palate, eyelids, nares, pharynx, larynx, and diaphragm, and attacks of uveitis. Possible diagnosis of disseminated sclerosis.

L. B., (J. H. H., 57571), a colored man 30 years old who worked as a stable boy, first came to The Johns Hopkins Hospital July 10, 1934, complaining of paralysis of the left side of the face. The patient had always enjoyed good general health. When he was twenty-seven he noticed that he was becoming emotionally unstable. A year later he was troubled with black specks before the eyes and dimness of vision. He spent two weeks in another hospital, and vision became normal again.

Three days before coming to the Johns Hopkins Hospital the patient awoke to find the left side of the face paralyzed. Examination revealed a complete paralysis of all the muscles innervated by the left facial nerve, a typical Bell's palsy. On August 28th the patient was reexamined. There had been considerable return of strength in the muscles of the left side of the face. Now the muscles of the lower portion of the face were weak on the right side. He said that his right arm and leg were becoming paralyzed, and the right arm felt abnormally warm. The deep reflexes on the right were hyperactive and there was a right Babinski reflex. He was admitted to the hospital.

Words were pronounced indistinctly. There was a snoring sound in breathing even when the patient was wide awake and sitting up. This may have been the first manifestation of the myoclonus which was then unrecognized. He was emotionally unstable and cried frequently. The right side of the soft palate was definitely weak. Mild but definite weakness of the right arm was demonstrated. The abdominal reflexes were absent bilaterally.

Laboratory tests revealed few abnormalities. The Wassermann reaction was negative in the blood and spinal fluid. There were 14 cells per cubic millimeter in the spinal fluid.

Three weeks after leaving the hospital he noticed that the left eye was red, and his vision blurred. He was troubled with diplopia and black spots in front of the eyes. Examination revealed injection of both conjunctivae. There was a hemorrhage in the macular region of the left retina. A scotoma was demonstrated in the left eye.

During the ensuing winter the patient spent a considerable period at the Baltimore City Hospital. At this time it was first noticed that he had palatal myoclonus. In August 1935 he noticed further weakness of his voice and of the right side of the body. The legs became so weak in November 1935 that for a month the patient was unable to walk. Both eyes, particularly the left, became inflamed. He was admitted to the Wilmer Eye Clinic for treatment of the acute uveitis.

The patient improved considerably and was not seen again till August 1937 when he complained of swelling of the right ankle. A month later he returned with pain in the left side of the head associated with dizziness. His gait became very unsteady, and speech was almost unintelligible.

The patient was examined on November 14, 1938 when the present studies were begun. He was well developed and nourished. The eyes were prominent. The right pupil was larger than the left; both were of regular outline. The right pupil responded well to light and on accommodation. The left pupil did not react to light directly but there was a consensual response. It did contract on accommodation. The right optic disc was flat, and pale on the temporal side. The media were cloudy on the left. The left disc showed primary optic atrophy. There was a well sustained nystagmus on looking to either side. Small irregular movements of the eyes occurred when looking forward.

The corneal reflexes were absent on both sides. The nasolabial fold was deeper on the left. The movements of the lower portion of the face were much stronger on the left than on the right. Nor did the right side of the face respond to emotional stimuli. Laughing was manifest only in the left facial musculature.

Bilaterally symmetrical rhythmical movements were seen in the eyelids and in the nares. Movements of the eyelids were more marked when the eyes were closed, especially when closed tightly. The contraction tended to pull the lids downward and inwards. When the breath was held, the movements became of much smaller amplitude but did not stop. They were increased in excursion with inspiration, particularly deep inspiration. Rhythmical movements of the nostrils were affected similarly by inspiration. Movements of the eyelids and nares did not stop during sleep.

There were also rhythmical movements of the perioral muscles. These were not as obvious as those in the nares but could be recognized clearly on palpation. The facial myoclonic movements were accentuated on the left side by voluntary contraction of the muscles.

The rhythmical contractions were particularly marked in the soft palate which showed bilaterally equal movements of considerable amplitude. These displayed little variation during inspiration or expiration. Similar contractions could be seen in the pharyngeal wall. No fast or slow phases of movement were observed. Voluntary contractions of the pharynx were weak. The uvula was swollen. No gag reflex could be obtained. If the observer's ear was placed near the patient's head, a ticking sound could be heard in the mouth which was synchronous with the palatal myoclonus. On deep inspiration the air was inhaled in a spas-

modic manner, producing a sobbing sound. There were no similar sounds during expiration.

Laryngeal examination showed that both arytenoids and vocal cords contracted in a rhythmical manner, both on phonation and when the patient held his breath. The movement of the cords was somewhat jerky, similar to movements seen when a normal person laughs. The orifices of the eustachian tubes opened and closed synchronously with the pharyngeal movements.

Speech was husky, harsh, and disturbed by poor coordination with breathing and by the rhythmical movements. There was a certain tendency to slurring of the syllables. When asked to utter a continuous "ah" the sound was interrupted by the myoclonus. The patient had to take his time when swallowing. He choked often, but had not regurgitated fluid through the nose. The tongue deviated to the right and was moved with difficulty to the left. It showed no rhythmical movement.

Although the patient was right handed, the grip was better on the left. In the finger-nose test there was mild ataxia which was greater on the left. When the patient was lying quietly there was little respiratory movement of the chest. On taking a deep breath the chest expanded with jerking movements. Fluoroscopic examination showed rhythmical movements of the diaphragm associated with respiration. The abdominal muscles were weak, particularly on the right. They appeared to move synchronously with the myoclonic contractions of the diaphragm.

The patient's gait was ataxic and slightly spastic. He tended to deviate toward the left. Station was unsteady and was impossible with the eyes closed; he always fell toward the left side. Both ankles showed some edema, more marked on the left. Power of dorsiflexion of the right ankle was weak. Ataxia could be demonstrated in the heel-knee test, especially on the left.

The deep reflexes in the arms were bilaterally overactive, especially on the right. Hoffmann's sign was present bilaterally. The abdominal and cremasteric reflexes were absent. The knee jerks were active; a greater response was obtained on the right. The right ankle jerk was normal, but the left was sluggish. Babinski's sign was elicited on both sides.

There were no significant abnormalities of sensation. Perhaps there was a diminution from the normal in the length of time that the vibrations of a tuning fork could be felt at the ankles.

The rate of the pulse and of the movements as seen in the alae nasi were compared. The pulse rate was 84 and the rate of the abnormal movements 63 per minute. The patient stated that the amplitude of the movements was increased when he was emotionally disturbed.

The abnormal findings may be arranged in groups dependent upon injury of different structures in the nervous system. The large left pupil may be correlated with the visual loss in this eye. The clouding of the media was the result of recurrent attacks of uveitis. Temporal pallor was seen in the right optic disc and primary optic atrophy on

the left. The nystagmus, ataxia, tendency to walk and fall to the left and certain of the speech disturbances may be attributed to disease of the cerebellum or its pathways. There was some injury of the corticospinal fibers which involved the right side of the body more than the left. These symptoms of diffuse disease of the nervous system developing progressively in a young man free from syphilitic infection suggest a diagnosis of disseminated sclerosis. Peripheral facial palsies and recurrent uveitis are not usually a part of this syndrome.

DISCUSSION OF RECORDS OF THE ABNORMAL MOVEMENTS

We have obtained graphic records illustrating the abnormal movements. The time marker records 5-second intervals. In making the records a method similar to that described by Kolb and Kleyntjens (1937) has been utilized. A balloon is placed over the portion of the body to be studied and connected by means of thick-walled rubber tubing with another balloon of smaller size inserted in an air-tight bottle. A rubber tube connects this bottle with a tambour, movements of which are recorded on a kymograph. Air is introduced until oscillations of the desired size are obtained. When simultaneous records of the two sides of the chest are desired, two of these systems are employed.

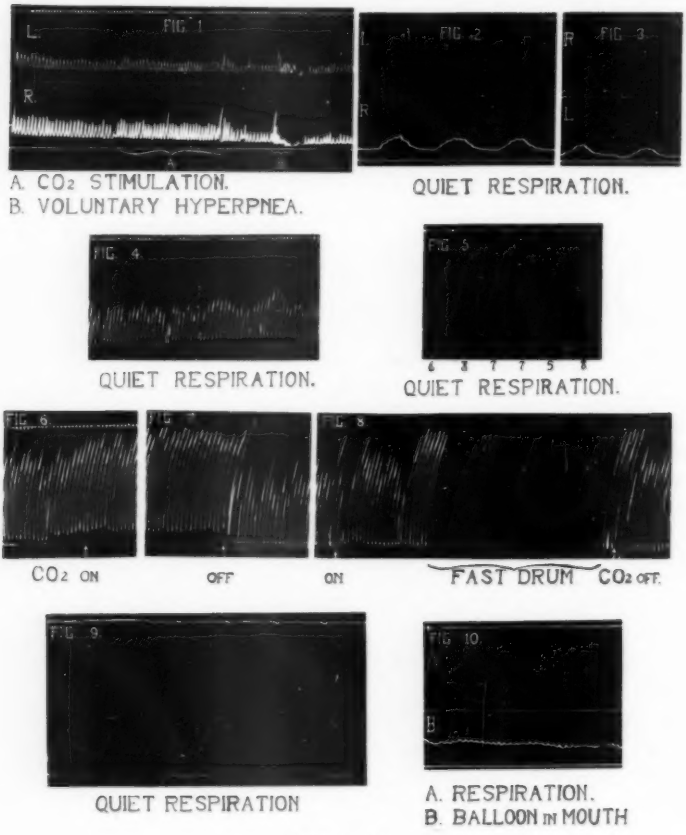
The first three figures show simultaneous tracings of the two sides of the chest. The balloons were fastened separately at the anterior axillary lines.

At the point marked A in figure 1, the patient was allowed to breathe carbon dioxide. The amplitude of movement was increased upon both sides. Voluntary hyperventilation was performed at B in the same figure. It may be noted that the voluntary inspiratory movements tended to tire more quickly on the right, the side of the hemiparesis.

Although the balloon systems were reversed between figures 2 and 3, it will be observed that the movement of the chest was always greater on the right. The kymograph drum of course revolved more rapidly in these records than in figure 1. Accordingly the myoclonic movements are seen more clearly. They appear to be more marked during and particularly toward the end of inspiration.

Figure 4 shows a period of quiet respiration. The single balloon

recording the movements was placed over the epigastrium. Slight irregularities at the peak of the inspirations indicate the abnormal waves. It will be observed that there is a certain rhythmicity in the



FIGS. 1–10

amplitude of the respiratory movements, although this is not conspicuous.

The relation of the amplitude of the abnormal movements to the respiratory phase is clear in figure 5. It also shows that it is impossible

during quiet breathing to count accurately the myoclonus by observing the alae nasi. One observer attempted to count the movements with each respiration as indicated by the numbers below the curve. The counts do not agree with the number of abnormal movements seen in the record. Moreover the myoclonic beats cannot be counted accurately even in this tracing.

Figures 6, 7 and 8 show the effect of carbon dioxide upon the respiratory rhythm. The amplitude is increased by carbon dioxide and the volume of the respirations is more regular. The respiratory rate is essentially unchanged. During the second period that carbon dioxide was applied (fig. 8) the speed of the drum was increased. The abnormal movements are seen clearly during inspiration.

The record in figure 9 is one of quiet respiration. In this particular record the myoclonus is evident during all the phases of respiration, although its amplitude is still accentuated at full inspiration.

In figure 10 (B) a balloon was placed in the mouth to record the movements there. Only a suggestion of change in amplitude of the movements with the different phases of the respiratory rhythm is seen. It will be noted that there is a fast component and a slow component of each contraction. The fast component represents contraction, and the slow, relaxation.

DISCUSSION

The abnormal movements are found in the facial area, involving the eyelids, alae nasi and the perioral musculature. They also occur in the soft palate, pharynx, larynx, and diaphragm. It is doubtful whether they are present in the extraocular muscles.

The facial muscles and particularly the muscles of the alae nasi are accessory muscles of respiration. In most of the reports which have been published the myoclonus was confined largely to groups of muscles used in respiration. However, one observer noticed alternate movements of pronation and supination in the right arm, and it is said that the fingers may participate in the myoclonus. The movements of the eyeballs which have been reported might result from injury of other cerebellar pathways.

It is well established that the lesion which produces the myoclonic syndrome involves the central tegmental fasciculus, inferior olivary

nucleus and their connecting pathways in the cerebellum. Sometimes the myoclonic movements are unilateral. When this is true they are manifest on the side opposite to the damaged olive. Davison, Riley and Brock (1936) who have summarized many reports, point out that the movements may appear on both sides even though the pathway is injured only on one. A possible explanation may lie in the fact that the respiratory movements are closely correlated on the two sides, and any disturbance of their integration is likely to be manifest bilaterally.

The rate of the movements has been most commonly noted as 120 per minute, though rates of 50 to 180 have been described. The frequency is constant for the individual patient; in our case it was about 60 per minute. Emotion or voluntary contraction increase the amplitude of the movements.

No satisfactory explanation for myoclonus has been suggested. Marinesco (1936) speculated as to whether it was due to irritative or release phenomena. He thought that myoclonus could be attributed to the suppression of a superior inhibitory control followed by freedom of automatic activity.

Freeman (1933) believed, from their tempo, rhythm, and constancy, that the movements were allied to the constant tremors of mesencephalic origin. They may be thought of as oscillations dependent on impulses from the corticobulbar neurones that have escaped normal control owing to destruction of extrapyramidal pathways.

Freeman pointed out the relation of the rhythmical movements to activity of the respiratory muscles. He discussed Wilson's theory that forced laughing and crying, observed in patients with pseudobulbar palsy, are due to release of emotional functions of the respiratory muscles.

The fibers of the central tegmental fasciculus end around the cells of the inferior olive, and in the myoclonic syndrome this nucleus shows signs of degeneration and often has a curious appearance of pseudohypertrophy. This group of cells shows changes in every case which has been examined. The fibers from the inferior olivary nucleus enter the cerebellum through the corpus restiforme.

It is possible that the rhythmic movements of the respiratory apparatus are similar to the other types of tremor associated with in-

volvement of the cerebellum or its pathways. A cerebellar tremor is characterized by the fact that it is increased by activity and is called an *intention tremor*. The palatal myoclonus has the characteristics of an intention tremor. Myoclonus may be considered to be a cerebellar tremor involving only selected groups of muscles, and related intimately to the destruction of one particular pathway associated with the cerebellum.

The central tegmental fasciculus passes downward from the region of the central gray matter around the third ventricle. Its origin has been placed by some in the thalamus, by others in the basal ganglia. Ranson calls it the thalamo-olivary tract. It may be intimately concerned with the uses of the respiratory muscles for emotional expression. The patient had a loss of the power of emotional responses upon the right side of the face.

Freeman was not certain that there was an associated mimic paralysis with the myoclonus. He reported two cases in which the movements were unilateral. In one, the face on the affected side no longer responded to emotional stimuli; in the other there was a general reduction in facial expression.

Almost all abnormal movements such as the tremor of Parkinson's disease stop in sleep. The myoclonus persists during sleep or anesthesia since it is an intention tremor and the respiratory muscles in which it appears are still contracting.

The abnormal movements of facial muscles, palate and pharynx contribute in large part to the difficulty of vocalization. Guillain (1938) pointed out that the speech showed abrupt pauses in the middle of a word or defective pronounciation of an isolated syllable.

The graphs show that the respiratory excursions are greater on the right side of the chest than on the left. There was a right hemiparesis and only slight evidence of involvement of the corticospinal fibers on the left. Kolb and Kleyntjens (1937) studied the movements of the chest in patients with hemiplegia. In those with marked increase in tone on the hemiplegic side, the respiratory excursions were decreased on that side. On the other hand cases with a flaccid hemiplegia had more marked movements of the chest on the paralyzed side. The spasticity in itself seems to limit the movements. If we omit the factor of increased tone, it may be postulated that the respiratory

center on the abnormal side is freed from some of its cortical stimuli and therefore responds more strongly to blood-borne stimuli and peripheral influences. This theory is confirmed by the effect of carbon dioxide which increases the amplitude of the respiratory movements on the hemiplegic side more than on the normal, whether the patient is flaccid or spastic on that side. The whole question of cerebral control of respiratory movements will be discussed in another place (Grimmer, Hesser and Langworthy, 1940).

Other abnormalities in the respiratory records may be attributed to diminution or loss of cortical control. During a series of voluntary deep inspirations there is a tendency for the movements of the chest to tire rapidly, particularly on the paralyzed side. Many patients with injury of the cortico-efferent paths on one or both sides show a rhythmicity of respiratory excursions. This is evident to only a slight degree in the present case (fig. 4).

We may speculate concerning the positions of the lesion in the nervous system producing the myoclonus in this case. It is probable that there are degenerative changes in the inferior olive on the right side. The changes in the dentate nucleus would then occur on the left. The cerebellar signs are more marked on the left side. The loss of emotional control of the face is on the right.

SUMMARY

The abnormal movements in a case of myoclonus occurred in the periorbital, alar, and perioral muscles and in the muscles of the palate, pharynx, larynx and diaphragm. There was a loss of emotional expression on the right side of the face and signs of cerebellar ataxia especially on the left. The myoclonus was increased by voluntary contraction of the facial muscles and during the active phase of respiration. It had, therefore, the characteristics of an intention tremor.

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STUDIES IN VITAMIN A

Relation of Vitamin A and Carotene to Serum Lipids[1]

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The anatomical changes of vitamin A deficiency are late changes, in the sense that before they occur, the vitamin stores are generally reduced to a point where they no longer exert their protective action. In experimental rats the stores have virtually disappeared by the time the first signs of deficiency appear. This is not necessarily true of humans, and it is likely that there may be other factors that supervene before the point of complete disappearance, preventing mobilization or leading to greater utilization or destruction so that the nonstoring tissues are not supplied rapidly enough to avoid depletion. In this connection there are two problems: (1) the recognition of dangerously depleted stores, and (2) the recognition of the factors that may lead to a breakdown of adequate distribution. The problem of the existence of symptoms arising from physiological changes associated with diminishing stores, cannot be attacked until we are able to recognize those cases in which the stores are actually diminished. The heated argument at present, regarding the value of the tests of adaptation to dim light, is due to the fact that we have not yet a method for determining storage deficiency; and not everyone agrees on the propriety of defining vitamin A deficiency in terms of adaptation tests.

The determination of the level of vitamin A in the blood is gradually coming to be used as a means of discovering whether the body is adequately or inadequately supplied with vitamin A. Studies on groups of individuals have shown a certain degree of correlation be-

[1] The photoelectric colorimeter used in this study was obtained with funds furnished by the Ella Sachs Plotz foundation.

tween the diet or social status and the blood level of vitamin A; and there is believed to be some general relationship between storage level and blood level, so that a low blood level is interpreted to mean some degree of deficiency. In the case of carotene, the level of which in the blood generally has a simple relation to intake, there is a point below which the figures are considered to be abnormally low. In the case of vitamin A, such a point has not yet been determined, partly because of the practical impossibility of correlating the blood level with the storage level, partly because of the absence of recognized symptoms associated with any state analogous to the so-called pre-scorbutic state of vitamin C deficiency, and partly because of the realization that there are a number of things about the vitamin A of the blood that are not yet understood; *i.e.*, there are factors other than the level of storage and intake, which influence the amount of vitamin A of the blood. It was to study these other factors that this work was undertaken.

There are a number of indications in the literature that the concentration of fat in the blood may have some bearing on the vitamin A or carotene level. Carotenemia has been found in those conditions associated with lipemia, notably, diabetes, hypothyroidism, and nephrosis (1, 2). A relationship between vitamin A and carotene and cholesterol in the blood has been reported (3, 4, 5, 6) by some investigators who have then gone on to explain the relationship on theoretical grounds, curiously enough ignoring the obvious fact that all three substances are soluble in fats.

The work reported here is a survey of the relation between total lipid content of the blood and the blood level of vitamin A and carotene The blood samples were obtained from patients suffering from a variety of different conditions. While an effort was made to obtain particularly high and particularly low lipid values in order to extend the curve as far as possible in both directions, there has been no extended study of any particular condition.

The chemical methods are given in detail at the end of the article.

RESULTS

Chart 1 demonstrates a relationship which has been discussed in the literature, namely that between cholesterol and vitamin A or carotene.

Chart 2 pictures the relation of carotene to total lipids. In spite of the scattering of figures, inevitable in this work, it is evident that there is a good correlation between total lipids and carotene. The position of the hollow circles representing cases in which the diet was considered inadequate in carotene, is probably due to the fact that the carotene value of the blood, in the absence of tissue "stores," depends to a large extent on the diet. The possibility that the fat of the blood may influence absorption will be discussed later. Although roughly

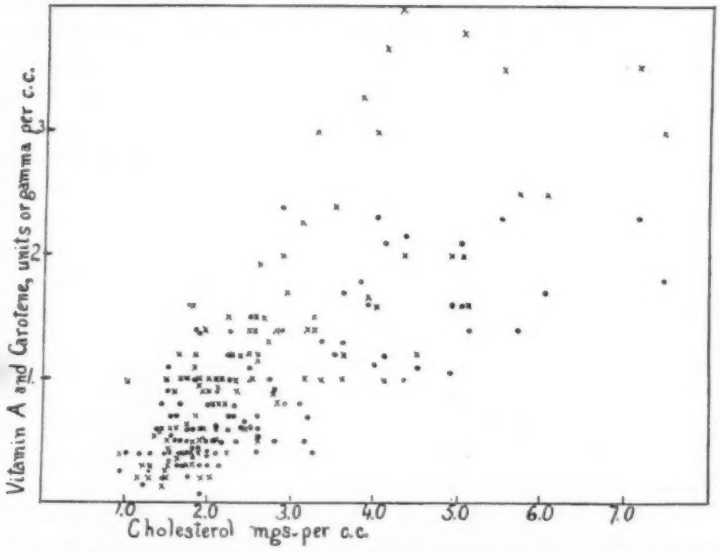

CHART 1. RELATION OF VITAMIN A AND CAROTENE TO CHOLESTEROL IN BLOOD
The dots represent vitamin A, the crosses carotene

50 to 60 gamma per 100 cc. may be taken as a level dividing normal from abnormally low, in judging adequacy of diets, it must be noted that in the presence of relatively high blood fat, carotene values as high as 80 may be obtained when the diet is inadequate, while in the presence of low blood fat, values below 50 gamma may have to be considered "normal."

Carotenemia, then, is in most instances a natural consequence either of the high blood fat with which it is so often associated, or of

a greatly increased intake, which may result in a great increase in the carotene of the blood without a corresponding rise in blood fat. There are cases, however, in which the carotene of the blood may be increased in the absence of either of these conditions, and apparently individuals differ considerably in the degree of carotenemia that may be produced

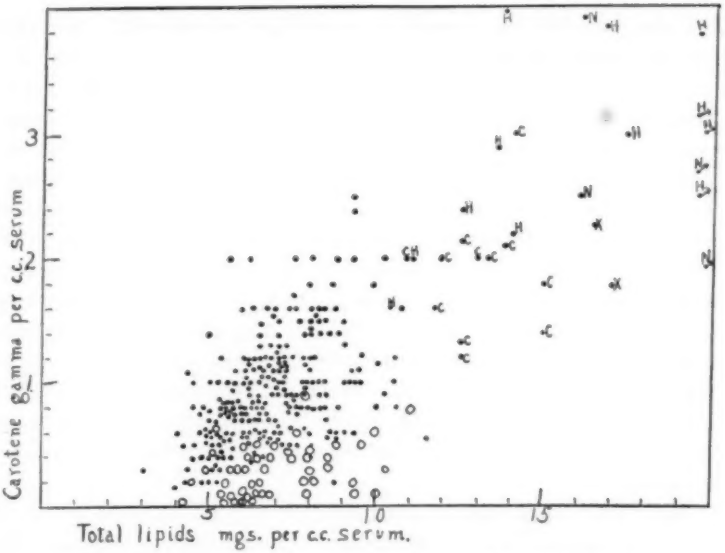

CHART 2. RELATION OF CAROTENE TO TOTAL LIPIDS OF SERUM

The hollow circles represent those cases, other than infants, in which the diet was judged to be inadequate in carotene or vitamin A. The diagnosis in cases with high serum lipid content has been represented by letters. *C* = cretinism. H = hypothyroidism. *N* = nephrosis. *X* = xanthomatosis. A number of these values lay outside the chart (designated by arrows pointing in the direction of the actual point in the extended chart).

in them by a given diet, and also in the amount of deposition in the skin associated with a given blood level. The slightly yellowish color in cretins is associated with a relatively high blood carotene; but in cases of nephrosis the yellowish tint of skin is lacking, though the blood carotene may be just as high. Two cases seen recently with markedly yellow skin and high blood carotene, had blood fat values above the

normal, to be sure, but not as high as are customarily found in cases of hypothyroidism and nephrosis.[2] This observation suggests that the level of blood fat may be a factor, since a high blood fat might conceivably hold the carotene in solution in the blood, while in the presence of a lower blood fat the carotene might be deposited in the skin more readily.

Chart 3 depicts the vitamin A—total lipid relationship. As in the case of Chart 2, in spite of the scattering, it is evident that there is a fairly close relationship between vitamin A and the blood lipids. Since the circles represent the same cases as in Chart 2, the conclusion must be drawn that the diet has less immediate influence on the vitamin A content of the blood, than on the level of the carotene. This was naturally to be expected owing to the fact that the storage of vitamin A is much greater than that of carotene. In the case of individuals voluntarily on a vitamin A free diet the carotene fell steadily almost from the beginning, reaching almost complete disappearance in two or three weeks, while the vitamin A remained at a fairly constant level for several months, and when it finally fell, the reduction of the level was relatively abrupt. In one case there was an abrupt fall during a mild upper respiratory infection, and a subsequent rise to the previous level when the infection was over, though the diet remained unchanged.

More than in the case of carotene, it is difficult to speak of a level dividing "normal" from "abnormal." The blood fat undoubtedly influences the vitamin A level and it may be that it is the concentration of vitamin A in the blood fat, rather than in the plasma or serum as a whole, that should be used as a criterion of deficiency. The cases included in this study in which there was reaon to believe that there might be some degree of deficiency, either because of the presence of other deficiencies (pellagra, alcoholic polyneuritis, nutritional edema) or because of an especially prolonged period of adaptation to dim light, were not sufficient in number to permit any conclusions on this point, but few as they are, they do tend to support this hypothesis.

[2] One of these patients had been on a high (but not excessively high) vegetable diet as a result of a faulty diagnosis of diabetes. In the other, no dietary factor could be found to account for the carotenemia.

The probability that vitamin A and carotene circulate in solution in the fat of the blood, has a possible significance in the interpretation of certain phenomena. The vitamin A-carotene-cholesterol relation has already been mentioned, and it seems likely that the relationship depends on the fact that all three are subject to the same factor,

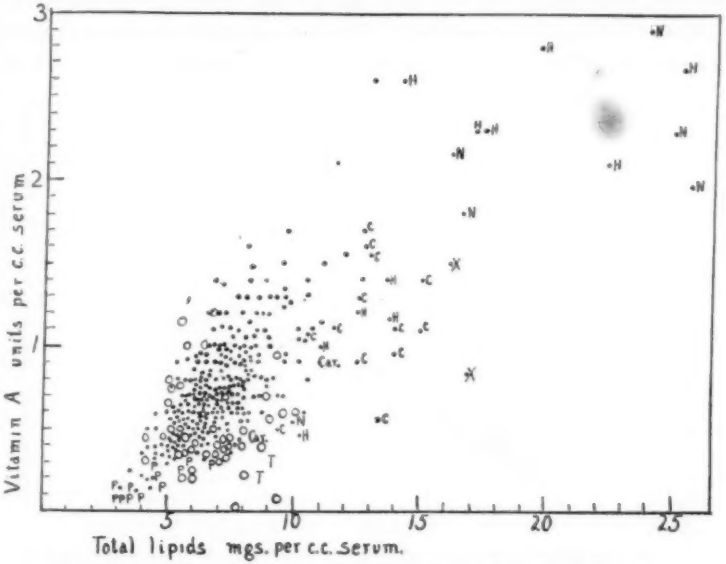

CHART 3. RELATION OF VITAMIN A TO TOTAL LIPIDS OF SERUM

This is the vitamin A in a "strict sense," *i.e.*, after correcting the obtained value for carotene, as described in the method for determination. The hollow circles represent the same cases as in the previous chart, *i.e.*, those with diets inadequate in carotene or vitamin A other than infants. The letters used in connection with the cases with high total lipid have the same significance as in the previous chart. The *P*'s in the lower left portion of the chart refer to cases of pneumonia in infants. *Car* refers to the cases with carotenemia and relatively low serum lipid, mentioned in the text.

namely, fat solubility. If this be the case, then the relation of total lipid to cholesterol should be a fairly constant one. This is shown in Chart 4. While it is not possible to state categorically that the vitamin A-cholesterol relationship depends merely on fat solubility, it is still necessary to guard against attributing a false significance to it.

Another aspect of the fat-vitamin A relationship is encountered in the interpretation of post-absorptive vitamin A curves. These have been used to gain information concerning intestinal absorption, especially in patients suspected of having celiac disease. A number of observations made for the purpose of studying the value of these curves, has indicated that their height and duration is greatly influenced by the fat of the blood. For if the blood fat is low, there may be almost no rise in blood vitamin A after ingestion of even a large

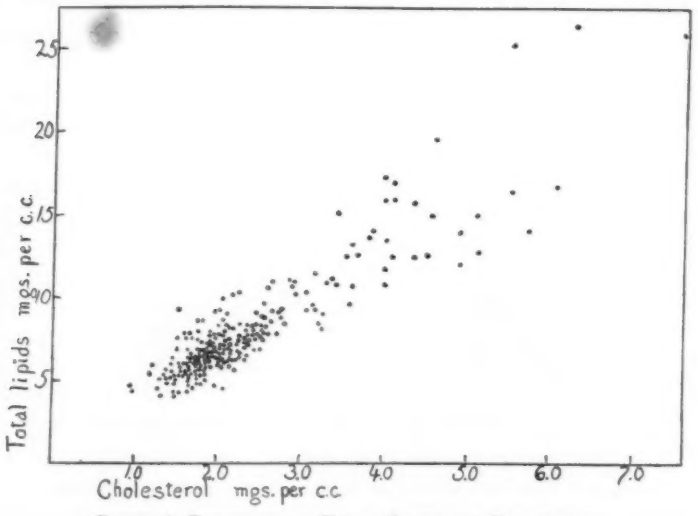

CHART 4. RELATION OF TOTAL LIPIDS TO CHOLESTEROL

amount of the vitamin (Chart 5). This does not mean that absorption may be an unimportant factor; but if the rate of absorption can be related to the blood fat, then one should not too readily assume that a "poor absorption" is due to some intestinal abnormality.

The highest carotene and vitamin A values in this series were obtained in the conditions associated with lipemia, namely, hypothyroidism, nephrosis and xanthomatosis.[3] There is no case of diabetic lipemia in the group, and the few cases of diabetes without lipemia

[3] The high blood carotene value of xanthomatosis suggests the possibility that the yellow color of the xanthoma may be due to local deposit of carotene.

showed nothing out of the ordinary. The lowest values were obtained in pneumonia in infants (but not in older children), in cardiac decompensation, and in patients with evidence of other deficiencies. In cases of pneumonia the low values were associated with low values for total lipids, and improved spontaneously with the rise in blood fat immediately after recovery. Likewise, in the two cases of cardiac decompensation the low values were associated with low blood fat.

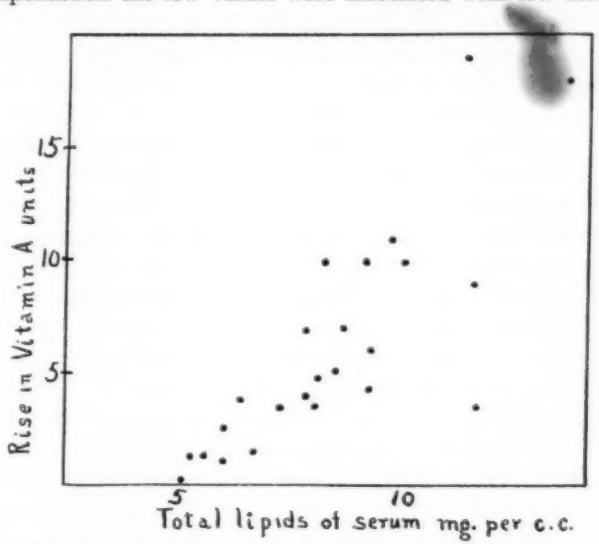

CHART 5. RELATION OF POST-ABSORPTIVE RISE IN VITAMIN A TO TOTAL LIPIDS OF SERUM

The rise in vitamin A is obtained by subtracting the initial value per cc. from the value obtained four hours after ingestion of 2 to 6 cc. of *Haliver Oil*, the amount depending roughly on the weight of the subject. Two of the lowest figures for the post-absorptive rise were obtained in normal adults.

In the cases of dietary deficiency, as already stated, low blood fat was not necessarily present. Infants with general malnutrition but without any specific evidence of deficiency of other vitamins were not among those with the lowest values.

It would be premature to attempt to draw any conclusions from these observations though there are certain obvious suggestions, namely,

that the concentration of the vitamin A in the blood fat may be more important than its concentration in serum in judging the state of the stores, and that a low concentration in the blood fat may interfere with the proper distribution to the non-storing tissues. Certain other suggestions may be made, but they have what might be called a negative value, in that they serve merely as deterrents to certain inferences that have been drawn without exploration of other possibilities. I refer especially to the inferences regarding the significance of the vitamin A-cholesterol relationship, and those regarding the interpretation of post-absorptive curves. It is not that the inferences may not be correct or at least "on the right track," but that they were made without consideration of possibilities such as are indicated in this work. Another inference falls into this category, namely, that in hypothyroidism the capacity of the liver to convert carotene into vitamin A, is reduced. This is based on the observation that in hypothyroidism the carotene-vitamin A, ratio in the blood is raised. *A priori*, it is just as reasonable to suppose that the increase in carotene is dependent on the high level of blood fat which holds it in solution and to that extent hinders its conversion. Much more should be known before an inference such as the foregoing, can be accepted as more than an untested possibility. The field of vitamin A research is already cluttered with ill considered attempts at generalization which have been widely accepted on no better recommendation than that of plausibility or attractiveness.

SUMMARY

A series of observations has been made correlating the blood levels of vitamin A, carotene, cholesterol and blood fat, as part of a study to determine the factors which must be considered in an interpretation of the vitamin A of the blood. The only conclusion to be drawn is that there is an obvious relation between vitamin A, carotene and total lipids of the blood, and it is suggested that the basis for this is the fat-solubility of vitamin A and carotene. It is not possible at the present time to conclude that the concentration of vitamin A in the fat of the plasma, is more significant than that in the plasma itself, though certain observations discussed in the article indicate that this is a possibility. The bearing that this relationship has on the interpretation

of some of the phenomena observed in previous studies of vitamin A is pointed out.

METHODS

1. Vitamin A and carotene determinations

The method is essentially that of Clausen and McCoord (8), in which vitamin A and carotene are extracted by means of petroleum ether from a mixture of equal parts alcohol and serum (or plasma or whole blood). The carotene is determined by color comparison with a standard, and the vitamin by means of the blue color formed by the addition of antimony trichloride dissolved in dry chloroform.

The antimony trichloride reagent was prepared by dissolving fresh antimony trichloride in dry chloroform so as to make a saturated solution at room temperature. If the chloroform is not absolutely dry a white precipitate forms from which the clear reagent may be decanted. Fresh reagent was prepared about every two months.

Two methods of determination were used. In one, the color comparison was made directly with a set of tubes of copper sulphate solution prepared in gradations from 10 per cent to 0.625 per cent (9 tubes in all). The tubes were 5 cm. in length and about 1 cm. in internal diameter, and were chosen to have the same calibre. To each of them were added 2 cc. of the copper sulphate solution. They were then calibrated with a commercial sample of *Haliver Oil* (Parke, Davis) the strength of which, in international units, was approximately known. The other method made use of an Evelyn photoelectric colorimeter calibrated with the same sample of *Haliver Oil*.

The procedure was as follows: 1 cc. or less of serum was pipetted into a clean Wassermann tube, made up to 1.5 cc. with water, and 1.5 cc. each of alcohol and petroleum ether were added. The tube was stoppered with a tightly fitting cork stopper and shaken at intervals for about 10 minutes. After centrifuging, the supernatant petroleum ether layer was carefully pipetted into a tube similar to those used for the copper sulphate solutions. The yellow carotenoid color was compared with carotene standards. These were made up in a series of tubes containing from 0.2 to 2 gamma dissolved in 2 cc. of petroleum ether. The comparison was made by looking vertically through the tubes. If the carotene tubes were kept stoppered in the refrigerator, they would maintain their strength for about two weeks, and then could be freshly prepared from a stock petroleum ether solution containing 100 gamma per cc. This stock solution was compared from time to time with a permanent yellow color made up from the dye used to color nucoa, which at the level of concentration represented by the stock carotene solution had the same yellow tone of the carotene. Slight deterioration in the stock carotene solution could thus be detected and a correction made.

When the carotene had been estimated, the tube containing the vitamin A sample was placed in a beaker of hot water, and the petroleum ether blown off

with a stream of dry air. 0.2 cc. of dry chloroform was added to dissolve the fat, then 2 cc. of the antimony trichloride reagent. The blue color was compared with that of the copper sulphate tubes, the final reading being made at thirty seconds.

If the photoelectric colorimeter was to be used, the petroleum ether-vitamin A solution, after the carotene estimation, was pipetted into a microcolorimeter cell, which was then placed in a dish of hot water and the petroleum ether blown off by

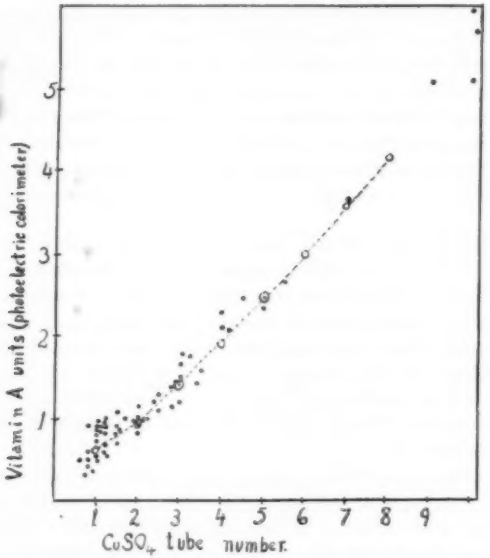

CHART 6. COMPARISON OF VALUES OBTAINED BY COPPER SULPHATE METHOD WITH THOSE OBTAINED BY PHOTOELECTRIC COLORIMETER ON THE SAME SERUM SPECIMENS

The dotted line represents the calibration of the copper sulphate tubes by means of freshly diluted *Haliver Oil* specimens, the vitamin A content of which was at the same time determined by the photoelectric colorimeter.

a stream of dry air. 0.1 cc. dry chloroform was added and the cell placed in the housing. 1 cc. of the antimony trichloride reagent was added and the galvanometer deflection determined.

The approximate accuracy of the copper sulphate method was determined by comparing the estimations with those made with the photoelectric colorimeter, as shown in Chart 6. The lower limit of the copper sulphate color corresponded to the color produced by about 0.6 units of vitamin A. Below that limit estima-

tions were a matter of guess-work, depending on a faint blue color that lasted 30 seconds, or on the speed with which the faint color completely faded.

The copper sulphate method was found useful for routine estimations where an approximation was all that was desired, and could be used in a study where knowledge of fine gradations was not necessary. The chief drawbacks of the copper sulphate method are (1) the fading of the color which becomes more rapid when the carotene component is high; (2) the fact that the color is comparable with the copper sulphate color only at relatively low concentrations and that a large proportion of carotene deepens the blueness of the color so as to make color comparison difficult even at low concentrations; and (3) the difficulty of knowing exactly when a comparison should be made with a continuously fading color. Following Clausen's suggestion, the time was arbitrarily taken at thirty seconds after the addition of the antimony trichloride reagent. This was satisfactory under ordinary circumstances, but was too long a delay when the color faded rapidly.

As is well known, the antimony trichloride reagent measures both vitamin A and carotene and it is necessary to determine how much of the blue color or galvanometer deflection is due to carotene. As stated above, both the blue color and the light absorption as measured by the galvanometer deflection, are expressed in terms of approximate international units. The blue color and the galvanometer deflection caused by measured amounts of carotene were also determined. It was found that 1 gamma of carotene corresponded to 0.4 units of vitamin A, and this is the value used in obtaining the figure for vitamin A alone. In other words we obtain a reading which represents vitamin A plus carotene but which we express in terms of units of vitamin A. We have already determined the carotene by means of its yellow color. With the conversion factor above we can express carotene also in terms of units of vitamin A. Subtraction of this figure from the other gives the value to be assigned to vitamin A alone.

2. Total lipid and cholesterol determinations

The total lipids were determined as follows: 1 cc. or less of serum was pipetted into 15 cc. Bloor's Solution (3 parts alcohol to 1 part ether) and heated in a water bath for about ten minutes, making up for evaporation with Bloor's Solution. After standing for an hour or two, the solution was filtered by suction into a 250 cc. filter flask and the precipitate washed twice with a small amount of Bloor's Solution. The flask containing the filtrate and washings was then placed in a hot water bath and the filtrate evaporated under a vacuum with a sufficient current of air admitted to prevent boiling and consequent spattering. When dry and while still hot, the sides of the flask were washed down with petroleum ether in four or five successive portions of about 1 cc. each. As soon as the flask had cooled enough to allow the collection of a small amount of petroleum ether at the bottom, this was transferred to a Wassermann tube. The flask was again washed down once or twice and the washings added to the same Wassermann tube. This was

centrifuged to throw down in a coherent mass any precipitate that might have been pipetted from the flask, and the petroleum ether was then transferred as quantitatively as possible without stirring up the precipitate to a clean dry weighed tube. This was then placed in a beaker of hot water and the petroleum ether evaporated off in a current of dry air. When dry, the tube with the fat was immediately weighed to 0.1 mg.

When cholesterol was to be estimated the fat was dissolved in chloroform, transferred to a volumetric flask and an aliquot used for the colorimetric determination.

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THE ELECTROENCEPHALOGRAM IN HEALTHY RELATIVES OF EPILEPTICS

The Constitutional Elements in "Idiopathic Epilepsy"

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The origin of the present study lay in the following accidental observation: William, Ruth and Carrol are the children of healthy parents. William, 15 years old, and Ruth, 12 years of age, are epileptic. For years they have been under ambulatory treatment in in the dispensary of the Harriet Lane Home of The Johns Hopkins Hospital, under the care of Dr. L. Kajdi. From time to time they have petit mal seizures, occasionally also grand mal attacks. Their brother, Carrol, who is now 9 years old, is apparently entirely normal. The parents, who from long experience with their two older children have learned to recognize the signs of the petit mal attacks and the importance of observing the children closely, both declare that Carrol has never shown even the slightest symptom suggestive of epilepsy. With a balanced temperament (as far as that can be said at all for a boy of his age), he is kind, pleasant and a good but not exemplary pupil in school.

The two affected children showed changes in their electroencephalograms (EEG) which are typical of epilepsy (1). Spontaneously, but especially after a short period of overventilation, there appeared long runs of spikes and waves often lasting for many seconds, and of huge amplitude. Usually these electrical spells were below the threshold of consciousness, and they were not attended by clinical manifestations. Carrol, who accompanied his brother and sister, was also examined. His EEG is shown in figure 2. The pattern as a whole was extremely irregular: slow waves of large amplitude and of a frequency between 3 and 4 per sec. predominated; faster components were almost entirely absent. The EEG is very much the same as we are

accustomed to see in patients whose complaints and symptoms put them in the borderland of epilepsy (2), or as we find it in cases of petit

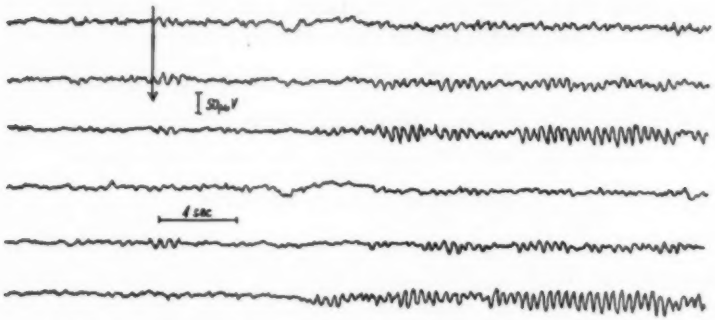

FIG. 1. ELECTROENCEPHALOGRAM OF A NORMAL, 26-YEAR-OLD MAN; CEREBRAL EURHYTHMIA

At arrow: closing of the eyes. In this and in the following graphs the reading is from left to right. From above: 1) fronto-precentral, 2) precentral-postcentral; 3) postcentral-occipital region of the left side; 4) fronto-precentral, 5) precentral-postcentral, 6) postcentral-occipital region of the right side. All calibrations are in microvolts.

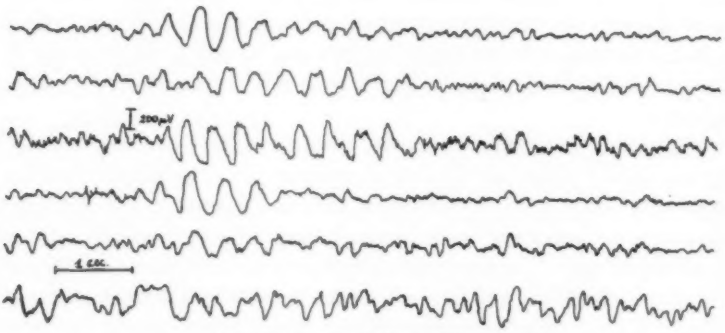

FIG. 2. CARROL FR., 9 YEARS OLD, NORMAL

Brother and sister epileptic. EEG, 2 minutes after cessation of 3 minutes of overventilation. Note the low amplification.

mal when the picture is changed by medication with phenobarbital or sodium bromide (3).

No studies have as yet been published on the electroencephalogram of the non-epileptic relatives of epileptic patients. However, in a paper which in general is dedicated to other problems Gibbs, Gibbs and Lennox state briefly that they examined "a family consisting of five members, only one of whom, a boy of 14, had symptoms of central nervous system disorders. He had petit mal. The other four members had no complaints but the father and the identical twin sisters had abnormality of rhythm which in all three was most pronounced in the right motor region." The authors speak in these cases of "potential abnormality" and differentiate between clinical and electrical abnormality (4).[1]

The whole matter demanded a broader investigation because of the importance of the clinical as well as the theoretical implications. All the relatives of our epileptic patients who could be reached easily were asked to come to the clinic to have their EEG taken. We tried, however, to get for examination many members of the same family-unit rather than a large general group of relatives of epileptics. We were more interested in obtaining a view into the principal facts, than in aiming at statistical conclusions.[2]

METHODS

The electroencephalograms were obtained in the usual way. Small chloridized silvercups were fixed on different points of the skull with collodion. As a rule 4 electrodes were placed on each side, over the frontal, the precentral, the postcentral and the occipital regions of the brain. A ninth "indifferent" electrode lay over the mastoid. From these electrodes the potentials were led off to Grass-amplifiers, and the changes were recorded simultaneously with six ink-writers.

Thirty-seven relatives of eleven epileptics were examined. In the family-unit which will form the basis of this report, fifteen members could be reached. Almost all of the persons examined were previously known to the Social Service Department, and it could in this way be ascertained whether we had really to do with persons which one could call "normal" with regard to epileptic or kindred diseases. Every person naturally was questioned during the session.

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[1] Since this paper has been in press these authors presented before the Amer. Neurol. Ass., June 5th, 1939, a paper dealing with "The inheritance of epilepsy as revealed by the electroencephalograph." In 55 per cent of the parents of epileptics one or both of the parents showed abnormal records.

[2] On this occasion I wish to express my thanks to the social service workers of the Henry Phipps Clinic and of the Harriet Lane Home for their invaluable help in inducing the different members of the families to come for examination.

RESULTS

It is, of course, impossible to present here the entire material. The demonstration, therefore, will be confined to two families whose records may serve as examples. Summarizing, it can be said that of the thirty-seven healthy individuals—or at least individuals who are *still* healthy—(who is able to say that the illness will not become manifest later?)—no less than seventeen had EEGs which must be considered abnormal. Four of them plainly had what may be regarded as "seizure" waves.

Edgar Mu. is the third child among nine siblings (Figure 3). He is now seventeen years old. He was seen first in the dispensary of the Phipps Clinic in March

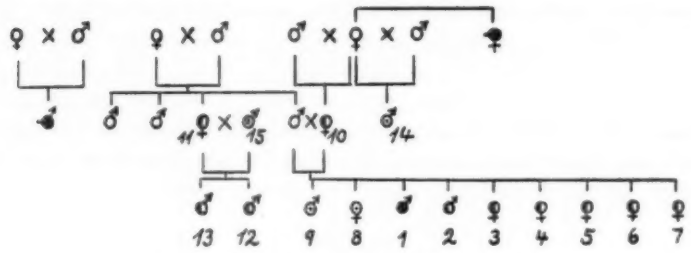

FIG. 3. FAMILY TREE OF THE MU. FAMILY

Numbers refer to persons examined. —●—manifest epileptic, no EEG available; ●—manifest epileptic, pathological EEG; ○—normal, no EEG available; ◐—normal, pathological EEG; ⊙—normal, normal EEG.

1935. Feeling well then, the boy was brought here in order to make plans for him after his father's sudden death. He had a mental age of 12 years and 4 months, was described as an alert and friendly personality and "good citizen-material," and was recommended to a training school for boys. In 1936 he had his first epileptic spell, a grand mal attack. These attacks became gradually more and more severe, his character deteriorated, and a few weeks ago he had to be transferred to the epileptic ward of the State Hospital.

Edgar's EEG was done in March 1939. Runs of 3-per-sec. spikes and waves over all regions, lasting sometimes up to 15 seconds, occur spontaneously and often. They are unaccompanied by clinical manifestation, and make his record a typical one for "idiopathic epilepsy" (Figure 4).

The *father* died 4 years ago in an accident. He is described as having been a normal and healthy man all his life. One of his cousins suffered from epilepsy. Nothing else of relevance could be elicited from his family-history.

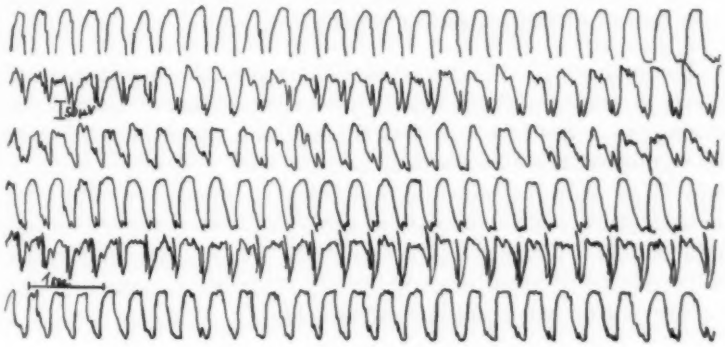

FIG. 4. EDGAR MU., 17 YEARS OLD. EPILEPTIC

Record taken during an "electrical spell" of which he is entirely unaware. Typical paroxysmal cerebral dysrhythmia: "spike-and-wave pattern."

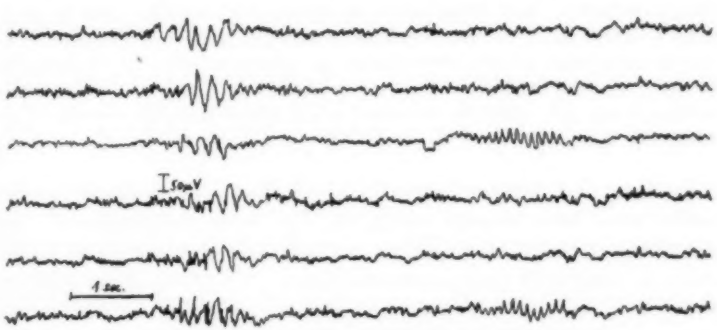

FIG. 5. EDGAR MU.'S MOTHER, 39 YEARS OLD, NORMAL

Spontaneous spike-and-wave eruption in an otherwise fairly regular pattern. Five similar disturbances appeared during a period of 4 minutes.

The *mother*, now 39 years old, married when she was 16. She bore eleven children, nine of whom are living. One child died at six months, the other, a hydrocephalic, was still-born. She has always worked hard and has felt well except on one occasion, in the winter of 1923, when she became nervous, irritable toward the children, and had trembling spells. This was obviously due to over-

work—she never had had any recreation—and no money difficulties. When these matters were straightened out and she had had a few weeks rest, she became again entirely well and has remained so since. Her father and her father's brother, she states, were heavy drinkers. The sister of her mother died in Springfield State Hospital with the diagnosis of "epilepsy."

The mother's EEG is characterized by a generally regular pattern, waves of small amplitude and almost entire absence of alpha-waves during rest. But here and there the regular features are interrupted by a group of slow waves with an amplitude not very large but markedly larger than the preceding and following waves, and with intermingled spikes. Overventilation, although it was continued for nine minutes, did not change this picture at all. No increase in the amplitude, and no decrease in the frequency of the waves occurred either during or after this procedure (Figure 5).

The *mother's half-brother*, No. 14 of the family tree, is a healthy man, and his EEG is normal. He has 12 normal children, but as yet none of them have been examined.

None of the two *brothers* and six *sisters* of Edgar has ever exhibited signs of epileptic behavior. Like Edgar before his sickness they are alert, friendly, good pupils in school and by no means different from other children of their age. Except for the younger brother whose mental age corresponds with his chronological age, they all have Intelligence Quotients above 100 per cent, and no abnormal findings of any sort could be discovered which would have any bearing on an "epileptic" disorder.

Yet, only the older brother and the older sister (Nos. 8 and 9 in the family tree) have records which are free from abnormalities. No disturbances appear during rest; nor are there slow waves or an increase in amplitude during overventilation. Of the younger siblings, every one has an EEG with a thoroughly irregular pattern, with waves of large amplitude and occasionally slow. The form of the slow waves is humped and notched; quick deflections, not quite so sharp as real spikes often precede them. In two of the children, Nos. 4 and 7 of the family-tree, 3-per-sec. spike-and-wave groups appeared either spontaneously or after a short period of overventilation. In the other four, overventilation produced 3-per-sec. waves with an amplitude exceeding, and usually far exceeding, 200 microvolts, which out-

lasted for many seconds the end of the forced breathing and recurred again and again in the course of the following minutes (Figures 6 and 7).

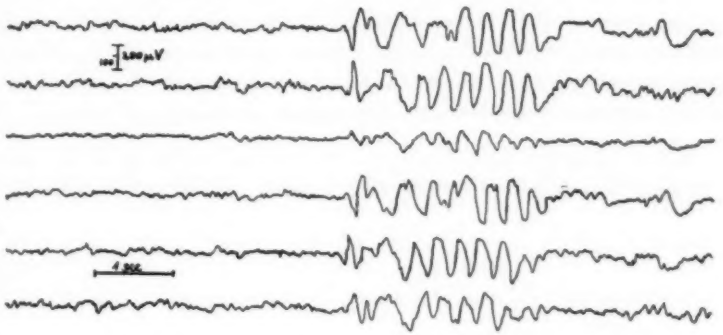

FIG. 6. EDGAR MU.'S BROTHER, 14 YEARS OLD, NORMAL (NO. 2)
At rest, eyes closed. Low amplification

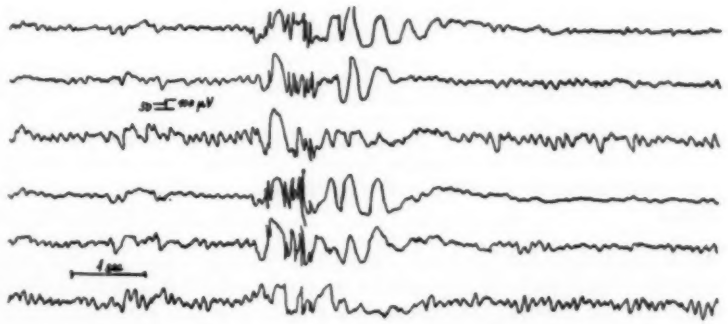

FIG. 7. EDGAR MU.'S SISTER, 12 YEARS OLD, NORMAL (NO. 3)
One minute after cessation of 45 seconds of overventilation; the third of 5 similar occurrences during 2 minutes. The same disturbances occur also during rest, but not so frequently. Low amplification.

Edgar's *paternal aunt*, Mrs. B., (No. 11) is a woman of thirty-four years, healthy, good-humored, balanced, clever and cooperative. She has no somatic complaints whatsoever.

The record of her brain activity, shown in figure 8, is abnormal. Even during rest she occasionally has a sudden wave of higher amplitude than the others; and often a short run of waves occurs with a frequency below 7 and 6-per-sec. but with the same amplitude as the neighboring waves. Overventilation for 4 minutes brings about a gradual change until 2½-per-sec. waves govern the whole picture. These waves persist for more than forty seconds after the end of the overventilation; there is then a resumption of the original pattern.

Mrs. B.'s little son, Edward, born in 1934, developed at the age of two years "breath holding spells." He would suddenly shriek, hold his breath until he got

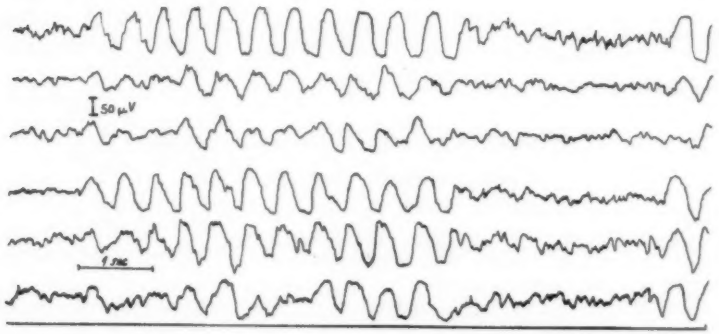

FIG. 8. EDGAR MU.'S PATERNAL AUNT, 35 YEARS OLD, NORMAL (NO. 11)

Two seconds after stop of 4 minutes of overventilation. The voltage does not quite reach 200 microvolts but the slow wave pattern is maintained for almost a minute.

rigid and fell, and would be a little shaky for half an hour. Afterwards he would not sleep. The attacks usually occurred when things were taken away from him, *etc.*, and it was therefore suspected that these spells were temper-tantrums rather than epileptic equivalents. Edgar had then had his first spells, and the boy was very closely observed with reference to the diagnosis "epilepsy." Since the spells in Edward were facilitated by the influence of the grandmother and a great-aunt living in the same house, the boy was put in a home for a few months. Here the spells disappeared entirely and have never reappeared.

Irregularities and sudden changes in frequency, form and amplitude of the curve during rest are the outstanding characteristics of Edward's EEG (Figure 9). Waves of large size and of a frequency of 3 or 4-per-

sec. follow upon a few deep breaths and last a long time after quiet breathing and a comfortable position have been resumed.

Edward's brother, Mason, now 13 years of age, is and always has been a normal and noisy boy, forming no problem at all for his parents.

The activity of his brain produces a regular EEG during rest. But the increase in the amplitude to over 200 microvolts and the long persistence of the continuous run of slow waves after 4 minutes of overventilation, reminds one of his epileptic relatives[3] (Figure 10).

The record from which figure 11 was cut out, was taken from a 40-year-old woman. She has no complaints. She is the mother of a

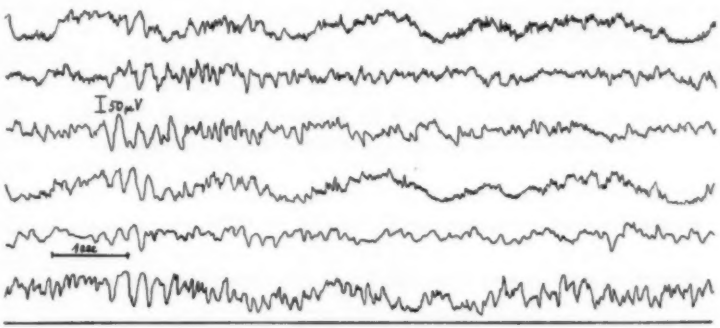

FIG. 9. EDGAR MU.'S COUSIN, 4 YEARS OLD (NO. 12)
At rest, eyes closed

normal 18-year-old boy and of an epileptic girl of 15. The latter's EEG is typical; it is loaded with long runs of 3-per-sec. spikes and waves in all leads, and in the intervals the pattern is irregular throughout.

In the mother's EEG groups of waves and spikes occur spontaneously, suddenly emerging in an otherwise regular pattern. Overventilation, unfortunately, could not be performed because the subject had a cold (Figure 11).

[3] The father's EEG was also taken for control. It was regular in its pattern. Overventilation did not produce any pathologic features. There was a slight tendency to form slower waves towards the end of the period but there were no runs nor was the amplitude of the waves beyond 75 microvolts.

From this woman's son a very regular rest-record was obtained and although the frequency of the waves slowed somewhat during

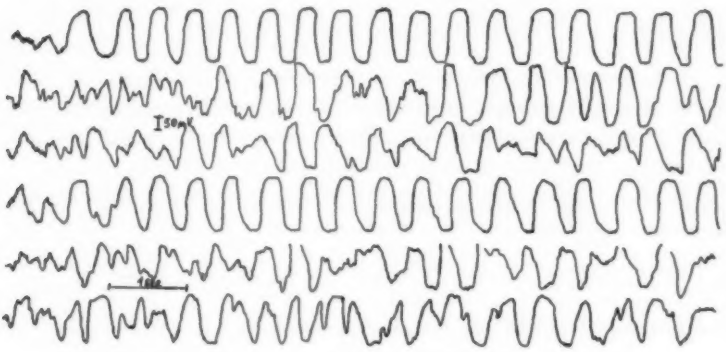

FIG. 10. EDGAR MU.'S COUSIN, 13 YEARS OLD, NORMAL (NO. 13)
Immediately after cessation of 4 minutes of overventilation

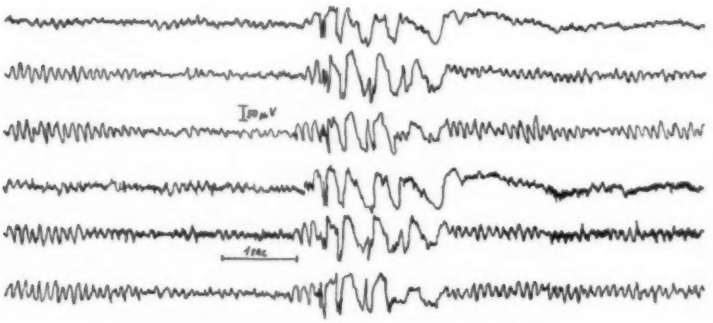

FIG. 11. MRS. BETTY PR., 40 YEARS OLD, NORMAL
Mother of an epileptic daughter and a normal son. Spontaneous spike-and-wave eruptions occurred several times during the examination.

overventilation and their amplitude became larger, these changes were within normal limits. The curves returned to their original shape almost immediately after the cessation of overventilation.

DISCUSSION

These examples must suffice to demonstrate what we have to deal with. As mentioned above, seventeen out of thirty-seven subjects yielded records which were abnormal beyond doubt. We have considered as abnormal all spike-and-wave groups regardless of the frequency, and all slow waves of a frequency of 3 to 4 per sec. provided they appeared spontaneously, or in long runs and for a considerable time after the end of an overventilation period, and provided their amplitude reached or exceeded 200 microvolts. These abnormalities were, as in epileptics, not restricted to any one area but were distributed over the entire brain.

Taking these signs as indicators of abnormality, we think we are safely outside of the range of what all authors have observed in the average "normal" person. With regard to the characteristic seizure-waves, Jasper and Hawke (2) have recently stated that "they were found only in patients with epilepsy or with some borderline epileptoid condition, and not in 200 patients with clearly non-epileptic disorders." Extensive examinations of normal unselected persons with exact family-data should be made in order to get a view of the distribution of such abnormal features. On the other hand, each person in whom signs such as are described above, are found, should from now on be questioned concerning epileptic disease in his family, even if he himself has not had epilepsy.

The question arises whether these electroencephalographic abnormalities are symptoms of epileptic disease which has not yet reached the threshold of clinical detectability, or whether they are merely the expression of a constitutionally unstable brain-activity which is characteristic for this type of individual. The following observation seems to favor the second of these explanations: We had the opportunity to examine identical-twin sisters, one of whom is epileptic while the other one is normal in every respect. They were born in 1927 in The Johns Hopkins Hospital and the delivery-history states expressly "single ovum." Their EEGs, too, were identical as Davis and Davis (5) have described in normal identical twins. A very irregular pattern with sudden changes in the generally high amplitude and with intermingled slow waves, were the essential features during

the resting period. Overventilation resulted in large 3-per-sec. waves which persisted in long runs for minutes after the cessation of the overventilation. Spike-and-wave groups were absent in both sisters. This seems to indicate that although both sisters have, of course, the same inherited constitution and therefore exhibit the same unspecific dysrhythmic brain activity, only one of them has acquired the other elements necessary to develop the epileptic disease.

We therefore draw the conclusion that it is no longer justified to look upon every cerebral dysrhythmia with the 3-per-sec. spike-and-wave pattern, as well as with large 3-per-sec. waves only, as unconditional evidence for petit mal, when we find the same paroxysms in healthy individuals without any indication of epileptic disorder. There are no means to tell from the EEG alone and without clinical information whether the records were obtained from a patient with petit mal or from a clinically normal person closely related to an epileptic. To the otherwise fortunate term "paroxysmal cerebral dysrhythmia" proposed by Gibbs, Gibbs and Lennox, should be appended: "with clinical signs" or "without clinical signs."

In practice, the importance of the spike-and-wave pattern remains, of course, unimpaired. Now, as formerly, the presence of this pattern will serve, in cases with convulsions of uncertain etiology, to exclude the diagnosis of psychogenic or symptomatic epilepsy. In several patients with hysterical convulsions we found, in agreement with other observers, that the electroencephalogram, which at rest was very regular, was entirely uninfluenced by hyperpnea.

Of greatest clinical interest is the problem of protecting constitutionally susceptible persons from the overt symptoms of epilepsy. But as long as the nature of the elements which lead to overtness remains unknown, we must be content to make further observations.

SUMMARY

A study has been made of the electroencephalogram of the normal relatives of epileptic patients. Out of the thirty-seven persons without any clinical sign indicating an epileptic disorder, seventeen showed an abnormal pattern, *i.e.*, waves which, during rest, were generally irregular, slow, and of high and uneven amplitude, and which, after a few minutes of overventilation, showed an increase in amplitude to

exceed 200 microvolts and a decrease in frequency to 3 to 4 per sec. The large slow waves persisted in long runs for a considerable time after the period of hyperpnea. Three of the individuals exhibited outright 3-per-sec. spike-and-wave groups regarded as pathognomonic of petit mal; one person had spike-and-wave groups of a higher frequency.

The question is discussed whether the abnormal features are a symptom of epilepsy which is still not severe enough to take the form of convulsions, or whether it is the expression of an inherited functional instability of the central nervous system, and, as such, nonspecific. From the observation of a pair of identical twins, one epileptic and one normal, both of whom have the same type of electroencephalographic records, it is concluded that the latter is the case, and that some other unknown factors have to be present besides the cerebral dysrhythmia in order to justify the clinical diagnosis "epilepsy."

Dr. Richard S. Lyman discussed this study frequently with me, and I thank him very sincerely for this opportunity and his many suggestions.

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FACTORS INFLUENCING PLASMA PROTHROMBIN IN THE NEWBORN INFANT

I. Prematurity and Vitamin K

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In 1937, Brinkhous, Smith, and Warner (1) reported that the plasma prothrombin level of the newborn, normal, term infant varied between 14 and 39 per cent of that shown by the normal adult. This work has been substantiated by Moore and Javert (2) who studied the relationship between maternal and infant prothrombin. By chance, both of these groups of investigators encountered one term infant in the course of their studies with an extremely low plasma prothrombin, and in each instance this was associated with hemorrhagic disease. It is the object of this investigation to extend these studies to include premature infants. The plasma prothrombin level has been determined by the method of Smith, Warner and Brinkhous (3, 4). Blood samples were taken from the antecubital vein of the mother and from the umbilical vein at the time of birth. The results are recorded in the tables below in units of prothrombin dilution.

In Table I, the plasma prothrombin level of eighteen mothers and nineteen full term normal infants is recorded. The relationship between the maternal and fetal blood levels agrees with that reported by previous investigators. In marked contrast with the findings in the normal term infants, are the extremely low values for the premature babies, shown in Table II. While the values in some premature infants tend to approach the lower level of those found in the normal infants, five out of the nine cases recorded have levels so low that they fall into the range reported for hemorrhagic disease by the above-mentioned workers. It is, therefore, not remarkable that one of these infants, H. C., died with multiple hemorrhages from the mucous mem-

[1] Fellow, National Committee on Maternal Health.

TABLE I

The plasma prothrombin levels of mother and child, expressed in dilution units, in eighteen full term deliveries

NAME	RACE	INFANT WEIGHT	PROTHROMBIN, DILUTION UNITS	
			Mother	Infant
E. R.	W.	3,920	85.8	20.0
E. W.	C.	2,470	124.4	22.7
M. S.	W.	3,110	144.0	34.4
B. T.	C.	2,675	46.2	14.2
M. C.	C.	4,015	99.0	36.5
E. B.*	W.	2,880 2,800	92.4	28.2 26.8
N. E.	W.	3,290	130.6	26.8
P. W.	C.	3,775	79.2	20.5
E. S.	W.	2,670	123.8	22.4
S. M.	C.	3,180	61.6	21.3
D. J.	C.	3,000	85.0	14.9
G. Z.	C.	3,400	97.4	13.8
M. C.	C.	3,120	45.8	14.0
M. B.	C.	3,500	45.0	14.8
B. H.	W.	3,800	150.5	28.6
J. G.	W.	3,620	129.8	15.0
Z. B.	C.	2,825	202.9	13.7
A. W.	C.	2,675	99.8	33.8
Average.....		3,201.3	102.5	22.2

* Double ovum twins.

TABLE II

The plasma prothrombin levels of mother and child, expressed in dilution units, in nine premature deliveries

NAME	RACE	WEEKS PREMATURE	INFANT WEIGHT	PROTHROMBIN, DILUTION UNITS	
				Mother	Infant
C. M.	C.	14	830		6.8
A. B.	C.	7	1,000	111.3	7.0
H. C.	W.	5(?)	1,545	79.9	5.0
E. E.	C.	6	2,275	121.8	14.0
E. M.	W.	3	2,120	175.9	11.2
R. W.	C.	3	2,335	65.9	6.7
P. C.	C.	5	2,130	123.3	13.4
J. D.	W.	8	1,210	207.3	10.9
D. A.	C.	12	1,735	130.0	0*
Average.....			1,686.6	126.9	8.3

* Amount of prothrombin too small to measure.

branes and gastro-intestinal tract 48 hours after birth, despite transfusion. The low plasma prothrombin levels of the normal term infants and the much lower levels found in the premature infants are in keeping with the well known fact that cerebral hemorrhage is the most common cause of neonatal death. Indeed, it seems probable that the small cerebral hemorrhages seen in full term infants after difficult operative deliveries, and in premature infants, even after spontaneous births, would be of little significance were the mechanism of clot formation undisturbed. However, any marked lowering of the plasma prothrombin would result in continued oozing from these areas and subsequent fetal death, or, at least, serious brain injury. With this in mind, investigations have been undertaken to discover means of raising the prothrombin levels of the newborn.

This attempt is being made in two ways: first, by feeding vitamin K[2] to the mother prior to delivery; and second, by feeding vitamin K directly to the premature infant. While it is too early to draw definite conclusions the results thus far are promising. Two mothers have been fed 3100 units[3] of vitamin K each day prior to delivery, one for sixteen days and the other for thirty days. The plasma prothrombin of the first mother was raised from 120 units at the onset of treatment to 274 units at delivery, while that of the second mother was raised from 94 to 158 units. Both of these mothers gave birth to full term normal infants; the first had a plasma prothrombin of 77 units, and the second a plasma prothrombin of 83.8 units. These levels are almost three times those reported for the normal term infant. Babies E. M. and E. E. (Table II) were each given 1000 units of vitamin K in their formulas every day for four days. On the fifth day of life the plasma prothrombin had been raised from 11.2 and 14.0 units at birth, respectively, to 33.0 and 82.1 units. This finding in premature babies is in accord with the contention of Waddell and others (5) that vitamin K is effective in shortening the prothrombin time in mature infants having low prothrombin levels.

[2] The vitamin K concentrate was furnished by the Squibb Institute for Medical Research.

[3] Ansbacher units (6).

SUMMARY

1. The average plasma prothrombin level in eighteen mothers and nineteen full term newborn infants was 102.5 and 22.2 units, respectively.

2. The average plasma prothrombin level in eight mothers and nine premature infants was 126.9 and 8.3 units, respectively.

3. Preliminary studies indicate that these extremely low infant prothrombin levels can be raised by feeding vitamin K to the mother prior to delivery, or directly to the infant after birth.

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BOOK REVIEWS

(The reviews represent the individual opinions of the reviewers and not necessarily those of the members of the Editorial Board of this Journal.)

Surgical Anatomy. By C. LATIMER CALLANDER. 2nd ed., entirely reset. 858 pp. Illus. $10.00. *W. B. Saunders Company, Philadelphia, 1939.*

Doctor Callander's book has rapidly been recognized as filling an important place in medical literature. It is well written, fully illustrated and arranged in such a manner that the important surgical facts of each region are discussed in the chapters describing that area. It has that all-too-uncommon quality of being practical as well as encyclopedic. It is an outstanding volume in its field and can be strongly recommended to surgeons, students and practitioners of medicine. The second edition is a thorough revision of the first, seen mainly in the condensation of the wording of the original, the elimination of obsolete procedures, and the addition of the newer developments which have taken place in surgical anatomy since 1933. This has resulted in a smaller and better book, containing more information, within some two hundred fewer pages.

R. T. S.

An Introduction to Materia Medica, Drugs and Solutions. By STELLA GOOSTRAY. 4th ed., revised. 184 pp. $1.75. *The Macmillan Company, New York, 1939.*

The objective of the author in writing this book which first appeared in 1924 was "to provide a textbook for the course in Drugs and Solutions as Outlined in the Suggested Curriculum of the National League of Nursing Education." Succeeding editions kept this main objective, added lists of general reference books and brought the material to date.

In this fourth edition the material has been entirely revised and cut somewhat since much of what was formerly taught in the course *Drugs and Solutions*, is now included in other courses in the curriculum.

It is the opinion of the reviewer that this volume is very valuable for students who are beginning a course in Materia Medica as well as for those who wish a review of the subject. The tabulation of *Drugs in Frequent Use* at the end of the book is most useful.

M. G. S.

The New-Born Infant, A Manual of Obstetrical Pediatrics. By EMERSON L. STONE, M.D. 2nd ed., thoroughly revised. 291 pp. $3.00. *Lea & Febiger, Philadelphia, 1938.*

The second edition of this valuable little book includes most of the advances made in the study of the new-born infant during the past decade. The obstetrician

and pediatrician will find it a useful introduction to the understanding of the newborn period. For the medical student and general practitioner it will serve as an adequate guide to the care of the young infant. It is written by a man primarily interested in obstetrics and the viewpoint toward the problems arising in the child just after birth is often colored by an intimate knowledge and understanding of the events just preceding birth. The chapters on the immediate care of the newborn and on breast feeding are especially good. One wishes that in considering the diseases and infections of the young infant the discussion of therapy could have been more complete. Many useful references are included in the text.

T. C. G.

Intern's Handbook. By Members of the Faculty of the College of Medicine, Syracuse University, under the direction of M. S. DOOLEY. 2nd ed., revised and reset. 523 pp. $3.00. *J. B. Lippincott Company, Philadelphia, 1938.*

This is a compact little volume, easily carried in a coat pocket. It deals briefly with almost every conceivable problem which might confront an intern and contains a great deal of useful information. But as a result of a wide diversity of topics it loses much of its value. Every hospital should have a book on poisons in the accident room, a book on laboratory methods in the laboratory; such sources of information are easily consulted and are far more valuable than the brief notes in this volume. From the educational point of view, too, it is perhaps not wise to attempt to simplify too much, matters which are fundamentally complex.

R. W.

The History of the Acute Exanthemata. By J. D. ROLLESTON. 114 pp. Illus. 7 s. 6 d. *William Heinemann (Medical Books) Ltd., London, 1937.*

This small book is a compilation of the material presented by Dr. Rolleston in the Fitzpatrick Lectures which he delivered before the Royal College of Physicians of London in 1935 and 1936.

It should be of value to every student, and to those physicians who are interested either in infectious diseases or in the history of such diseases, because it outlines in a brief but very satisfactory manner the history of small pox, chicken pox, scarlet fever, measles and German measles.

This publication is very "readable" and is well documented thus making it possible for the student who desires to inquire further into the subject to go directly to the original sources.

P. H. L.

Surgical Pathology of the Diseases of the Mouth and Jaws. By ARTHUR E. HERTZLER. 248 pp. Illus. $5.00. *J. B. Lippincott Company, Philadelphia, 1938* (Hertzler's Monographs on Surgical Pathology).

This volume is the tenth and apparently the last in a series of monographs on surgical pathology. Like its predecessors, it is written from a rich personal experi-

ence, and for that reason it possesses clarity, directness, force, and the usual pungency which comes from the facile pen of a versatile author. Dr. Hertzler assumes the attitude that his own acquaintance with diseases of the mouth and jaws is so extensive that it embraces everything which is of importance to the surgeon. Nevertheless, he salves his conscience by adding at the end of each chapter numerous references many of which have been selected by his secretary from the *Cumulative Index*. Obviously and unfortunately this type of book cannot be complete, and yet for all practical purposes it will satisfy the average surgeon. Exception may be taken to the brevity with which some of the infections are treated.

The material is arranged simply and in an orderly fashion. The numerous illustrations are well chosen, and, with two exceptions, are all photographs. Especial mention should be made of the excellent clinical photographs of lesions within the mouth.

F. C. L.